

‘Accept no limits’: Imaginaries of Life,  
Responsibility and Biosafety in  
Xenobiology

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## **Declaration**

I, Alberto Aparicio de Narváez, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

This thesis has been proofread by a professional editor who has made no contribution to the intellectual content of the thesis or been involved in rewriting text.

Date: June 24, 2019

*In memory of my parents, Guillermo Aparicio and Clemencia de Narváez.*

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## Abstract

Researchers in the emerging field of xenobiology aim to explore the non-canonical (or non-natural) biological world through the development of alternative genetic systems and chemistries. This discipline may help us better understand the origin of life, as well as enable the development of biological systems with built-in safety features (biocontainment). The development of xenobiology is assumed to be guided by goals, narratives, imaginaries and visions of possible futures, whose 'opening up' and examination are the central question of this thesis. This thesis combines work in science and technology studies and 'responsible research and innovation.' It focuses on the values, assumptions and "sociotechnical imaginaries" that drive the development of xenobiology, in terms of how xenobiologists understand and redefine life, and how they construct promises of biosafety through biocontainment. The thesis' argument draws on semi-structured interviews with scientists in the fields of synthetic biology and xenobiology. In addition, I conducted a year-long participant observation in a xenobiology laboratory located in London.

This thesis argues that two sociotechnical imaginaries lead the development of xenobiology. The first is about redefining life, or "life unbound," according to which the biological universe is thought to include (or navigate) novel biological worlds. Second, an imaginary of 'controllable emergence' accounts for claims of biosafety and governance by containment, a response to the collective imagination of the public who are fearful and concerned about release, and portrays scientists as responsible by pursuing safety. As xenobiologists test the limits of what is biologically possible, they also test the limits of what is socially acceptable. I describe how xenobiologists, in order to justify research in their field, draw on existing legacies of governance, such as the Asilomar Conference, and previous controversies over genetically modified crops. These legacies are still in use because they allow scientists to turn questions about governance into questions about design and science. These assumptions, shared by science funders, help to attract resources and visibility to the field, as well as legitimize the release of genetically modified microorganisms. This thesis concludes by suggesting that xenobiology should be open to uncertainty and frameworks that give up control in exchange for deliberation and reframing of problems as technologies advance, following ideas of real-world experimentation and collective experimentation.

## Impact Statement

In this thesis, I analyse a subfield of synthetic biology, termed xenobiology, with tools from STS. Xenobiology aims to construct organisms whose genetic code is expanded or recoded, and with nucleic acids not found in nature. This is an ultimate form of engineering life, defying our current conceptions of the boundaries between the biological and the synthetic, or a 'second biology,' reconfiguring the conception of organisms and their ecosystems. In addition, pioneers of the field have made promises to develop safe-by-design, 'biocontained' genetically modified microorganisms, incapable of transmitting genetic material to 'natural' organisms. I explore the visions and motivations of research in orthogonal biology, questioning how the field aims to shape social life and how scientists conceive the role of society in their agendas; implicit in this question is how to best govern such emerging field, questionings its value choices, implicit assumptions and epistemological judgments.

I aim to contribute to the literature on governance of emerging technologies and more specifically, responsible research and innovation, a framework implies that joins together societal actors during research processes in order to better align both the process and its outcomes with the values, needs and expectations of society. Scientists aim to position xenobiology as a responsible solution for a perceived problem of biosafety, which requires a nuanced understanding of how they see their role as scientists in society, how they conceive the public, and how they address responsibility. Through my research I have engaged with scientists through participant observation in a synthetic laboratory, aiming to bring society 'back into the laboratory' by raising difficult questions that touch on ethical, political and social aspects. The goal has been to raise reflexivity in scientists, so the results of their research are beneficial for society. This is particular important in an era of increasing lack of trust across many pillars of society, in government, media and financial institutions, and where the role of science has been disputed by post-truth politics that undermine the importance of facts to concede for emotional appeals is on the increase. Past technoscientific controversies across different sectors, from nuclear energy to genetically modified crops, call for rethinking the relation between science and publics.

The legacy of the scientists I have worked with during this research will attest to the impact of this study. Above all, I expect to provide a better picture of the barriers for thinking responsibly in science and the cultural narratives and imaginaries that sustain certain practices and behaviours in the scientific community, in particular with synthetic biologists. I also contribute toward thinking about frameworks for governance that acknowledge the uncertainty inherent in biological processes. Xenobiology serves as a mirror to observe the

values that are incorporated in new technologies and ask whether they are taking us to a desirable future. Hence, this research will be beneficial for establishing policies for science, technology and innovation not only in Europe, but globally where cutting-edge research is supported.



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# 1. Introduction

## 1.1 Introduction

Advances in the life sciences in the last decades have profoundly changed the social fabric of our world. Rapid technological advancement, mastery over nature, has left little time for reflection to make sense of how our relationship with nature and the world has changed, and will continue to change. Such changes have occurred in an atmosphere of promises or revolutionary medical advances that have not been fulfilled (Brown & Michael, 2003). Nevertheless, the hope of scientists that technology will improve our lives has sustained enough momentum, allowing new scientific fields to arise. In this day and age, where scientists strengthen their grip over life, with cutting-edge technologies that allow the manipulation of life with a surgical precision, like gene editing, it is important to understand how scientists think about life, and by extension, their duties and roles in society. For this task, I examine the goals, narratives, imaginaries and visions of possible futures made possible by the field of *xenobiology*, an umbrella term (Rip & Voß, 2013)<sup>1</sup> referring to a discipline in the life sciences oriented toward the ‘exploration’ of the non-conventional biological world, through the development of alternative genetic systems. Xenobiology, for those unfamiliar with the term, has been defined succinctly as:<sup>2</sup>

A subfield of synthetic biology, the study of synthesizing and manipulating biological devices and systems. Xenobiology derives from the Greek word *xenos*, which means “stranger, guest.” *Xenobiology describes a form of biology that is not (yet) familiar to science and is not found in nature.* In practice it describes novel biological systems and biochemistries that differ from the canonical DNA-RNA-20 amino acid system (see central dogma of molecular biology). For example, instead of DNA or RNA, XB explores nucleic acid analogues, termed Xeno Nucleic Acid (XNA) as information carriers. It also focuses on an expanded genetic code and the incorporation of non-proteinogenic amino acids into proteins (emphasis added).

With the power to extend the boundaries of life comes great responsibility. In this thesis I analyse the rhetoric, tactics and discourses that xenobiologists use to legitimize and justify research in the field, following their ideas of what the public needs and accepts. Furthermore, as scientists guarantee xenobiology to be a strategy to enable the release of microorganisms in open environments, plenty is revealed about barriers and dynamics between scientists and society. This in turn, that can inform debates on governance toward a more responsible

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<sup>1</sup> The authors write: “there is not only a struggle for recognition (and funding) of new fields within science, but also a struggle for legitimacy and resources in direct interaction with policy communities and a variety of social groups who are looking for opportunities to endorse and fund interesting research programmes.” (Rip & Voß, 2013: 43).

<sup>2</sup> Definition found in the Wikipedia entry for ‘Xenobiology’. Retrieved from <https://en.wikipedia.org/wiki/Xenobiology> [last visited 26 September 2018].

development of emerging technologies. How responsibility is incorporated into technological design has been overlooked, and this thesis aims to fill the gap in this regard.

The idea of a common attribute between all organisms on Earth share has entertained the imagination of scientists for decades. From the discovery of DNA as the molecule of inheritance and its double helical structure in the mid-twentieth century, scientists have experimented with alternative molecules to DNA that also support genetic information storage and transfer. One such finding in xenobiology and the study of life outside the boundaries of biology, was that DNA and RNA are not the only molecular systems capable of storing genetic information (Eschenmoser, 1999). Conceiving that the genetic code or the chemistry of the genetic system could be different is as old as early studies in molecular biology following the discovery of DNA as the molecule of heredity. Edward L. Tatum, winner of the Nobel Prize in Physiology or Medicine, stated in his Nobel Prize Lecture on December 11, 1958:<sup>3</sup>

With a more complete understanding of the functioning and regulation of gene activity in development and differentiation, these processes may be more efficiently controlled and regulated, not only to avoid structural or metabolic errors in the developing organism, but also to produce better organisms.

Perhaps within the lifetime of some of us here, *the code of life processes tied up in the molecular structure of proteins and nucleic acids will be broken. This may permit the improvement of all living organisms by processes which we might call biological engineering* (Emphasis added).

Tatum suggests a fascination with the ‘code of life’ and a willingness to manipulate as much as biology allows it. In this thesis I explore the scientific efforts to redefine what we understand as life and the boundaries between the natural and the artificial. As scientists try to rethink life, they also rethink discourses about how to fit new organisms (or possibilities) into society, mobilizing a set of promises, narratives and discourses of legitimation. I refer to narratives as a combination of constructs that people use to understand social phenomena and guide their actions. The scientific enterprise of constructing a ‘second nature’ is also displayed as a responsible action, as scientists they portray their approaches to biology as a safe technological path. In a commentary about the draft opinion on risks of synthetic biology conducted by the European Commission (EC) Scientific Committees, Breitling and colleagues (2015: 107) write that the European Union recommended for the improvement of the ‘safety locks’ of genetically modified organisms, the “development of additional approaches, including genetic firewalls based on noncanonical genetic material.” Such approaches can only be accomplished with xenobiology, a field that can provide control as a form of isolation, and thus safety.

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<sup>3</sup> From [https://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1958/tatum-lecture.html](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/tatum-lecture.html) [Last visited 21 June 2018]

In addition to studying the birth of the discipline (Bensaude Vincent, 2013; Powell et al., 2007), I focus on the discourses and imaginaries that sit behind efforts to redefine the genetic systems of living organisms (i.e., Benner & Sismour, 2005; Marlière, 2009). Given that all living organisms share the same genetic molecule of life, DNA, xenobiology involves the exploration of how life could have been different. Organisms on Earth may not share the same cellular properties, nor the same genetic codes, but one thing is certain: all existent forms of life share the same common ancestor(s) (cf. Woese, 1998) and are based on DNA or RNA (in the case of viruses). The success of synthetic biologists (or xenobiologists) in expanding the genetic basis of life changes our conception of the living. Such a profound transformation in how we approach life has the potential to reconfigure the social order in ways yet to be imagined. I ask what is at stake with this new field, not only about how it transforms the way we think about life, but what political and ethical aspects need to be considered if these new ways of thinking are to be adopted by society. In doing so, xenobiology offers a mirror of how scientists think about the public, and what type of values, prioritizing risk and safety, are legitimate. Conversations about new technologies tend to be framed in terms of whether new objects present hazards, and whether these hazards can be managed. Such inclination to evaluate and predict risk leaves a blind spot for questions of whether or not technology supports a good life, what kind of society we want to build with the help of technology, and who has a say in such paths that are being opened.

Particularly telling is the relationship between xenobiology and biological containment (biocontainment), the confinement of pathogenic and genetically modified organisms. Xenobiology employs two forms of biocontainment (cf. Torres et al., 2016; Wright et al., 2013). The first is auxotrophy, a nutritional requirement for organisms that cannot manufacture a nutrient by themselves. An organism cannot survive if it does not ‘eat’ a nutrient that it does not produce. In the case of xenobiology, such nutrients are artificial and cannot be found in nature. This has been used in molecular biology as a traditional tool, on the basis of mutants that cannot synthesize certain amino-acids. The second strategy corresponds to making it impossible to transfer of genetic information between organisms of different species. This has been a major concern about the environmental impact of genetically modified organisms, for example the transfer of antibiotic resistance genes to species in the wild.

A good way to illustrate auxotrophy and biocontainment is the fictional ‘lysine contingency’ fiction employed in the Michael Crichton’s novel *Jurassic Park* (New York: Ballantine Books, 1990). In the film adaptation, after the dinosaurs have escaped their cages, the park staff has an emergency discussion on how to handle the situation. Looking for solutions, the game warden Robert Muldoon asks, “what about the lysine contingency? We

could put that into effect.” Then the visiting paleobotanist Dr. Ellie Sattler asks what the lysine contingency is. Subsequently, CEO and creator of the park John Hammond says, “It is absolutely out of the question”” Afterwards, chief engineer Ray Arnold (played by Samuel L. Jackson) states:

The lysine contingency is pretended to prevent the spread of the animals in case they ever get off the island. Dr. Wu inserted a gene that creates a single faulty enzyme in protein metabolism; the animals can't manufacture the amino-acid lysine. *Unless they are completely supplied with lysine by us, they slip into a comma and die* (Emphasis added).<sup>4</sup>

Unfortunately, the lysine contingency biocontainment mechanisms did not spare the visitors of the park them from facing terror by dinosaurs wreaking havoc on the island. Because safety is also the result of human agency, and institutions and technologies are unruly (Wynne, 1988), the containment mechanisms in Jurassic Park not only failed to imagine uncertainties that the system could present but also to respond to such external hazards. This film sheds light on a theme that runs throughout this thesis: how risks are imagined in biotechnology and addressed via technical features like biocontainment or safety-by-design, key features of the governance of sociotechnical systems, for which I claim that giving up the illusion of control is an important consideration for knowledge production and the actors involved.

For the task ahead I employ theoretical tools and methods from the discipline STS, a field known for its social constructivist approach (cf. Hackett et al., 2008). STS focuses on how scientific knowledge and technological systems are constructed (Sismondo, 2008), and considers science as a social activity shaped by history, institutions, beliefs, and values. The emerging field of xenobiology involves construction at many levels, in terms of bringing novel organisms into the world (with meanings that are yet to be understood), their fitting into the existing realm of living beings, and their portrayal as *safe* organisms. The type of inquiry in STS is devoted to finding alternative explanations, fighting reductionism and destabilizing or challenging dominant narratives, as well the visions of possible futures that technologies help realize (Jasanoff, 1996).

In this chapter I provide an overview of xenobiology and the context surrounding the claim of biosafety. I explain why STS provides a set of theoretical tools and empirical studies that are useful to study xenobiology from a social and political angle. Proponents of xenobiology aim to redefine the genetic basis of life, and in doing so, they also bring up past controversies over genetically modified organisms. They bid on the future of the field based on a negotiation of the limitations of modifying the natural, and assumptions on what the

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<sup>4</sup> From <https://www.imdb.com/title/tt0107290/quotes> [last visited July 5, 2018].



public may want or allow. Further examining these dynamics further lies at the heart of this thesis.

In the next section, I introduce the emerging field of xenobiology by referring to the *First Xenobiology Conference* (XB1) held in 2014, where leading scientists gathered to discuss common questions and goals of manipulating the genetic basis of life. In this conference, questions of ethics and responsibility were intertwined with the origin of the field, as the two are inseparable.

Subsequently, I address the main research questions that have guided the development of this thesis and its relation to STS and governance of technology. Next, I explain efforts of incorporating safety features as the characteristics or properties of a product, along with the consequences that this brings to governance and allocations of responsibility. Then I illustrate that xenobiologists have sought to provide solutions to the problem of safety and risks of genetic engineering as developing biocontainment, and the importance of studying this connection between technology and safety. Last, I provide an outline of the chapters in this thesis.

## 1.2 Xenobiology and the first xenobiology conference

XB1, the *first Xenobiology Conference*,<sup>5</sup> held from May 6-8, took place in Genoa, Italy, where visions of xenobiology were laid. The conference gathered a few dozen researchers from different regions of the world and diverse scientific disciplines, from synthetic biology to organic chemistry. Foundational conferences usually serve to define what set of questions researchers share, and how to advance the field forward. The ‘synopsis’ section of the conference website provides an overview of its focus, as follows:

Xenobiology (XB) is the endeavor to overcome the constraints imposed by evolution on natural living organisms. It is an emerging field in the context of synthetic biology, encompassing the design, generation and evolution of alternative forms of life. The *foundational conference* XB1 aims to gather scientists, engineers, designers, policy makers and other stakeholders to chart the paths toward an entirely novel biodiversity.

A major goal of the XB1 conference participants will be to assess how alternative life should be designed to reserve human health and the environment. With this in mind, sessions of XB1 will be devoted to plan experimental tasks for diversifying nucleic acid propagation, reprogramming proteins, expanding metabolism and assembling ecosystems *de novo*. The prospect of further diversifying the Earth’s biosphere *challenges current worldviews and raises new ethical and philosophical issues* while stimulating industrial innovation and artistic creativity.

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<sup>5</sup> A relevant source was the website <http://xb1genoa.com/> [Last visited March 16, 2017] (which is no longer available online). See also the video titled “The XB1 Conference” (hosted in *Vimeo* website platform), uploaded July 1, 2014 by BioFactor’s account – <https://vimeo.com/99627227> [last visited March 12, 2017].

The venue for the XB1 conference was chosen in the hope that Genoa's illustrious citizen Christopher Columbus will *inspire the exploration of yet unknown continents of life*<sup>6</sup> (Emphasis added).

From the moment of its foundation, xenobiology was stamped with a label of *navigation*. The Austrian non-profit Biofaction<sup>7</sup> prepared a short videoclip about XB1<sup>8</sup> that captures the desire of xenobiologists to redefine life and positioning themselves as responsible. The videoclip opens with Phillipe Marlière saying, "There was a momentum among different scientists all over the world, and we felt that it was time to organize a xenobiology conference." Glorious baroque classical music followed, setting the scene for the replica of a beautiful galleon stationed in the port of Genoa; after various close-ups to the ship, Marlière continues:

Biologists now are like navigators in the Renaissance, because we don't know enough, but we can move away from the natural world, and try to reach virtual continents of life, so to speak, so Christopher Columbus, appears as the icon for organizing this first xenobiology conference. And where was Columbus born? He was born in Genoa. That's where we are.

It is no coincidence that Genoa was chosen as the venue for XB1. It fits well within the narratives and metaphors that Marlière uses (as I explain in **Chapter four**). For him, xenobiology involves a departure from the natural and the familiar. This sail into uncharted territory that can bring many rewards, including safety. The Biofaction video also features Markus Schmidt, who explains the fundamentals of xenobiology and the exploration of the unknown:

We wanted to bring together some of the most important scientists working in the area of xenobiology, so this is kind of an inaugural conference... Xenobiology, the xeno stands for something foreign, something that is unknown, and biology is the science of life. To hear that there is to create and design and make in the laboratory forms of life that are not known from nature. *So it's life as we don't know it* (Emphasis added).

Later in the video, Phil Holliger, programme leader at the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, and pioneer in xenobiology, comments on the foundations of xenobiology, by saying,

One of the key things that xenobiology will tell us about is *if the chemistry of life is in some way special*, functionally privileged, superior to other chemistries that we might think of. Or if really, if life sort of arose in an opportunistic way, making use of the building blocks that were available, and building on that. So I think that is a truly fundamental question in biology to understand that (Emphasis added).

The fundamental questions in biology that xenobiologists aim to address are tied to questions of scientific responsibility, in the sense of effectively managing the hazards that the

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<sup>6</sup> See footnote 5.

<sup>7</sup> Biofaction is a non-profit organization that communicates and engages with public debates about synthetic biology, founded by Markus Schmidt, a major spokesperson in xenobiology. For the organization's website, see <http://www.biofaction.com/> [Accessed March 12, 2017].

<sup>8</sup> See Vimeo, video titled "The XB1 Conference", uploaded July 1, 2014 by BioFaction's account. <https://vimeo.com/99627227> [Accessed March 12, 2017].

technology may bring, constituting a tension and a relationship that I address in this thesis. For the short length of the video (7:35 minutes) the authors included opinions on matters of risk and implications for society of xenobiology; it is expected that such an emerging field raises eyebrows about its ethical ramifications, but having scientists being so upfront about their handling of responsibilities and consequences is remarkable. The scholar in Responsible Research and Innovation (RRI) René von Schomberg who participated in the conference (cf. Owen, Macnaghten, & Stilgoe, 2012; von Schomberg, 2013), comments in the video that an emerging technology needs additional personnel involved to oversee those producing of the technology because scientists and engineers do not often do risk assessment. Additionally, Markus Schmidt comments on responsibility in xenobiology. He sees his role in is “to ensure that right from the beginning, the societal and ethical issues are taken into account when developing this field, so that the field is developing in a responsible and conscious manner.” From the very beginning xenobiologists aim to incorporate responsible practices. Near the end of the video, von Schomberg comments on the importance of involving key stakeholders in discussions about trajectories of technology (cf. Von Schomberg, 2013):

Governments have a role as a regulator but very much more in emerging fields, as a facilitator for discussions and networks with stakeholders, to create environments where the stakeholders take up responsibility for their roles in innovation processes.

The video finishes with Marlière indicating an open path for xenobiology. Its future will be shaped by those who are brave enough to steer it: “I think it is far too early to fix the thinking, the directions, the navigation. We should just let people spontaneously go where their taste and intelligence tell them to go.” Is there a role for responsibility in a field that will be defined by the will of brave scientists? Leaving aside the excitement for science that xenobiology offers, I wonder whether and how xenobiologists conceive *limits*. Should the field be allowed to flourish as it may, or is there a role for social scientists and laypeople to influence its development? In order to address these questions, we need some clarity about what scientists understand as xenobiology. In fact, xenobiology not only conveys a set of foundational questions, but also aspirations of how science is disseminated in society and the power of scientists to impose one trajectory over others.

Philippe Marlière is a good reference to explain the ambitions of xenobiology, because he and other pioneers like Markus Schmidt and Piet Herdewijn gave the field its name and have promoted it actively.<sup>9</sup> Commenting in an interview with French science journalist Anna

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<sup>9</sup> See Herdewijn & Marlière, 2009; Marlière, 2009; Schmidt, 2010.

Musso<sup>10</sup> on the seminal paper of Romesberg lab in 2014 (see **Appendix one**),<sup>11</sup> Marlière defines xenobiology while referring to its aspirations. Hence, the nascent field of xenobiology is not only a set of epistemic assumptions, but is also wrapped up with value judgements and aspirations.

In Europe, the field in question is organized under the name of xenobiology. Xenobiology does not have an applied goal itself, it consists in conceiving, assembling and evolving living organisms, for the moment, of bacteria, so that they differ in their chemical organization from all the species of terrestrial ecosystems. Also this artificial biodiversity is totally captive of the environments where it is cultivated and incapable of contaminating, genetically polluting natural habitats. From the point of view of environmental protection, this is a path that can lead us to the ultimate protection.

Moreover, Philippe Marlière has articulated a succinct definition (coining a similar phrase to Markus Schmidt earlier): “Xenobiology is the study of foreign organisms, life as we do not know it.”<sup>12</sup> As I shall explain later, this foreign portrayal of life is associated to increased biosafety. Nevertheless, Marlière aims to propagate a vision for xenobiology that not all researchers in synthetic biology share.<sup>13</sup> Few researchers would identify themselves as xenobiologists. Xenobiology is not a consolidated discipline: it does not have a journal, a dedicated society, or a course of study (i.e., a doctoral programme). Most scientists active in the field would not label themselves as xenobiologists, because their disciplinary affiliations lie elsewhere, such as synthetic biologists, metabolic engineers, biochemists, organic chemists, molecular biologists, and so on. It takes plenty of work, including forging alliances and mobilizing resources, for heterogeneous scientists to be grouped under a single label. However, the realization of two conferences dedicated to xenobiology,<sup>14</sup> and the usage of the term in scientific articles, means there are ideas mobilized around a core set of assumptions and aspirations centred around xenobiology. Although I have heard comments in the course of my fieldwork that xenobiology is a terrible label for a discipline because of its association

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<sup>10</sup> Interview by Anna Musso. *La création d’organismes artificiels protégerait l’homme et la nature*. May 23, 2014 See: <http://www.humanite.fr/philippe-marliere-la-creation-dorganismes-artificiels-protegerait-lhomme-et-la-nature-533716> [Accessed March 7, 2017; translated via Google Translate website (revised for accuracy)].

<sup>11</sup> The article reported the creation of a semi-synthetic organism, a bacterium that uses the four canonical DNA bases (A, T, C and G), but that also holds in its genetic code a pair of two synthetic bases called X and Y.

Read more at: <https://phys.org/news/2017-01-scientists-stable-semisynthetic.html#jCp> (Last visited September 30, 2018).

<sup>12</sup> See footnote 10. This resonates with an episode of the TV show *Star Trek*, in which the crew of the Enterprise space ship is exploring a planet in search of life, and the ship’s surgeon Dr McCoy says: “it’s life, Jim, but not as we know it.” See Gee, 1999.

<sup>13</sup> Despite synthetic biology having its own set of epistemological assumptions, among them making biology easier to engineer, the boundaries between xenobiology and synthetic biology are not at all discrete. Many researchers in xenobiology identify as synthetic biologists. This may be explained by the associated prestige and institutional achievements that synthetic biology has obtained, like doctoral training programmes, university departments, and dedicated funding.

<sup>14</sup> Such as the XB1 conference in Genoa in 2014, and the second xenobiology conference, held in Berlin, 2016. See footnote 5.

with ‘xeno’: The xeno in xenobiology refers to the non-terrestrial nature of the exploration and developing life forms that are constituted by artificial genetic systems.

An important term to introduce is ‘XNA,’ for *xeno*-nucleic acid, or any type of nucleic acid different from DNA or RNA (**Figure 1**). Herdewijn & Marlière (2009: 792) refer to XNA as “additional types of nucleic acids (XNA for ‘xeno-nucleic acids’), whose chemical backbone motif would differ from deoxyribose and ribose, and whose polymerization would not interfere with DNA and RNA biosynthesis.” Vitor Pinheiro & Phil Holliger (2012: 245), citing Herdewijn & Marlière (2009), refer to XNA as any “synthetic genetic polymer with a focus on those that have shown potential for either chemical and/or enzymatic replication.” Notably, one of the first experimenters with alternative genetic systems, Steven Benner, does not employ the term ‘XNA’, but “artificial DNA-like molecules” (Benner, 2004: 625). Nevertheless, xenobiology is not restricted to the study of XNA nucleic acids in biological systems. Researchers also study DNA chemical variations, which maintain the core skeleton of phosphate and the sugar deoxyribose, but with different nitrogen bases. It also comprises the expansion of the genetic code (i.e., expanding from three to four nucleotides, or the reconfiguring the genetic code, so that codons code for different amino-acids or for amino-acids not found in nature (see **Appendix one**). Seen in this way, the xenobiology conferences play a role in unifying diverse approaches in biotechnology and biosciences under a set of goals and research questions, a unity which may lead to a more efficient attraction of resources and prestige.

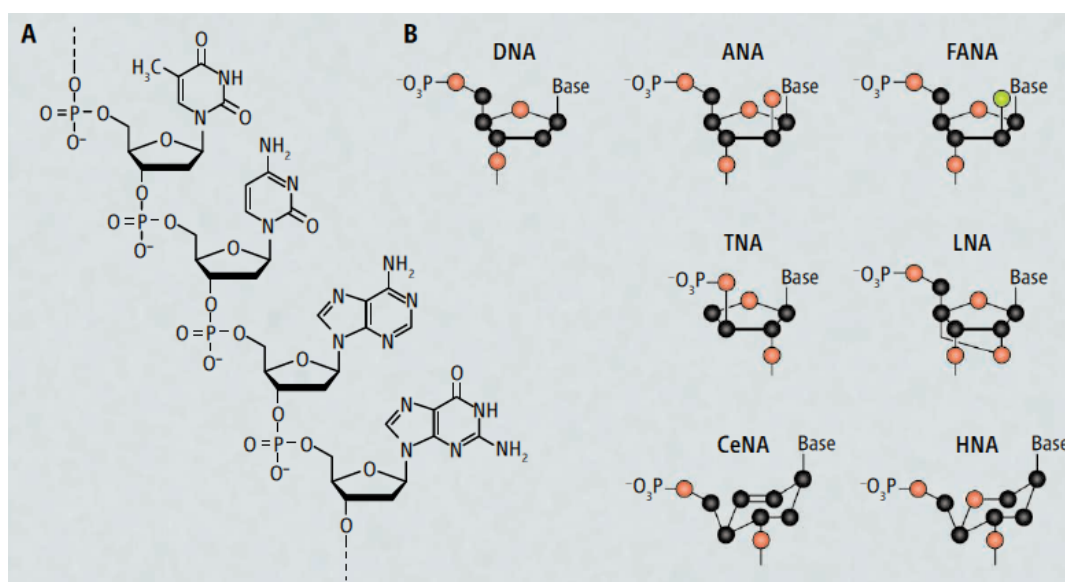


Figure 1. Illustration of a Deoxyribonucleic acid (DNA) chain (A) and (B) xeno-nucleic acids, information-storing biopolymers that differ from DNA in their ‘sugar’ backbone. Source: Joyce, 2012.

The field of xenobiology (also referred to as *orthogonal biology*) is relatively new, although its foundations trace back to the birth of molecular biology in the 1950s. It is one of several

disciplines that employ synthetic biology approaches (ERASynBio, 2014).<sup>15</sup> For the Engineering Biology Research Consortium (EBRC), synthetic biology “aims to make biology easier to engineer. Synthetic biology is the convergence of advances in chemistry, biology, computer science, and engineering that enables us to go from idea to product faster, cheaper, and with greater precision than ever before.”<sup>16</sup> It is gaining notoriety in policy circles (e.g. Carter et al., 2014; Pauwels et al., 2012).<sup>17</sup> For instance, one of the “radically new approaches” in synthetic biology (European Parliament, 2012: 211), associated with safety in genetic engineering (German National Academy of Sciences, 2010).

### 1.3 Research questions

This thesis aims to gain a better understanding of scientific practices in xenobiology, exploring its value choices, implicit assumptions, visions, narratives, and epistemological judgments, through engagement with synthetic biologists; and to provide insights on how emerging technologies can be governed responsibly. I emphasize on how the problems and promises that arise in xenobiology are constructed, such as the engineering of organisms with built-in biological containment features, and the sociotechnical imaginaries (Jasanoff, 2015a; Jasanoff & Kim, 2009) that support them. Sociotechnical imaginaries drive technological trajectories, represent visions of how technology should be developed for good or bad and more importantly, guide how states support visions of ‘where-to-get-to’ (see **Chapter two**).

I analysed an emerging technoscience (xenobiology) using a combination of qualitative research methods. The data I analyse and present in this thesis comes from a series of thirty-four semi-structured interviews conducted over one year (in 2016); this was complemented with participant observation in a synthetic biology laboratory (located in the UK) for one year, where I also led discussions with researchers about crucial topics about science and society related to xenobiology. In addition, I analysed policy and scientific literature about advances in the field and reflections about biosafety and biocontainment. I also attended academic events (i.e., conferences, workshops, seminars) about synthetic biology and xenobiology.

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<sup>15</sup> These approaches include Metabolic engineering, Minimal genomes, Regulatory circuits, Protocells, Bionanoscience and Orthogonal biological systems (what I refer to in this thesis as xenobiology). See also Acevedo-Rocha (2016) for a classification of the different subfields in synthetic biology.

<sup>16</sup> From <https://www.ebrc.org/what-is-synbio> [Last visited September 22, 2018]. Note that EBRC was formerly called SynBERC, a center established in 2006 to coordinate efforts between universities and private enterprises with the goal of making biology easier to engineer.

<sup>17</sup> The absence of discussion of xenobiology or orthogonal biology is telling in landmark reports such as Balmer & Martin, 2008; BBSRC & EPSRC, 2011; Presidential Commission for the Study of Bioethical Issues, 2010; Royal Academy of Engineering, 2009.

In this thesis I analyse the narratives, imaginaries and visions associated with xenobiology as a field that expands the boundaries of life and biosafety, fulfilling a promise of biosafety (through biocontainment). This relationship offers a prime view of how scientists conceive their responsibility to society and frame of problems to be solved via technology. I aim to show that xenobiology and biocontainment are supported by an expectation of achieving control over biological systems, which, in turn, will ensure public acceptance. In doing so, I provide elements to think about responsibility in emerging biotechnologies like xenobiology as giving up control, embracing uncertainty, and shifting the level of analysis from the organism to the ecosystems level. Following real-world experimentation (Gross, 2010a; Krohn & Weyer, 1994), which considers scientific practice as an experiment in which we are all inevitably involved, I call for a more open discussion of the purposes of innovation and how technologies are political in the sense of restricting (public) participation. If biocontainment serves to affirm certain assumptions and goals of biotechnology, like developing biosafe organisms or improving intellectual property control, I argue that by questioning such connections with xenobiology, we can develop opportunities to rethink the governance of biotechnology, to think less about risk and more about values and the public good. In the last section of this thesis, I challenge scientists and analysts to examine the different ways uncertainty and experimentation appear in the real world, arguing in favour of giving up control and adopting frameworks for governance that are both adaptive and inclusive.

Overall, this thesis contributes to the literature on the governance of emerging technologies, and responsibility in science and “Responsible Research and Innovation” (RRI) (Stilgoe & Guston, 2017). The analysis I present can contribute to the understanding of what motivates scientists and how they conceive responsibility, as well as the cultural resources (i.e. narratives, visions and sociotechnical imaginaries) they use to legitimize their research. Such cultural resources and ways of relating to society tend to be transversal to emerging technologies, not only relevant to the life sciences. Second, this thesis contributes to highlight the importance of *imagination* in scientific practice and risk management, as an important subject of enquiry.

Xenobiologists not only have the power to redefine the boundaries of life, but to extend humanity’s control over death and life and redefine (biological) time and space. A first theme to address in this regard is that of thinking of xenobiology as a point of reference to question a culture (or paradigm) that is pro-innovation,<sup>18</sup> one in which innovation is admired, believed to bring economic growth and solutions to pressing issues, without exploring their consequences, or how it may erode existing norms, a characteristic of the *moderns* (Latour,

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<sup>18</sup> For example, see Sveiby, Gripenberg, & Segercrantz, 2012.

1993: 41). Second, conversations about xenobiology raise questions about the purpose of the field (Guston, 2013) —at the heart of responsible research and innovation frameworks (cf. Stilgoe, Owen, & Macnaghten, 2013). Macnaghten & Chilvers (2014: 543) write in the context of public dialogues about science and technology in the UK, “When it comes to upstream processes, stated public concerns suggest a need for more deliberate consideration of political economic dimensions, the underlying motivations of science and scientists, and the potential for new science to disrupt natural orders.” Asking what motivates scientists to undertake research in xenobiology opens opportunities to extend the range of actors involved in the development of the field, since it destabilizes the status quo that technology must be developed for its own sake, in favour of a more democratic governance.

Third, looking at visions of the future serves as a mirror of past controversies. The study of xenobiology needs to include the social and historical context in which the field is embedded. This connects with what Michel Callon calls “overflows” (Callon, 1998): the negative externalities of science and technology, not necessarily restricted to accidents. Overflows are inevitable and cannot be contained with existing political and economic institutions, which allows the rethinking existing boundaries in society, particularly between experts and laypeople. Overflows often lead to controversies associated with outputs of technology, like genetically modified organisms (GMOs), Bovine Spongiform Encephalopathy (BSE), nuclear waste, mobile phones, the treatment of household waste, asbestos, tobacco, or gene therapy, that scientists and politicians try to avoid (Callon, Lascoumes, & Barthe, 2009). Nevertheless, Callon and colleagues approach overflows differently, welcoming the controversies as opportunities to explore uncertainties and “zones of ignorance;” they welcome the involvement of actors who would be excluded from participating and framing the stakes. As we shall explore in more detail, xenobiology aims to accomplish the opposite: to cease debate through achieving full safety of GMOs.

The analysis of the questions I present need to be considered in the context of biotechnology. For instance, the controversy of genetically modified crops in Europe in the late 1990s (cf. Bauer & Gaskell, 2002; Gaskell & Bauer, 2001), manifested through the regulatory procedures that delayed or restricted commercial use of genetically modified crops, leading to public protest and outrage. Kearnes and colleagues (2006: 301) provide a wider explanation of why genetically engineered crops were rejected:

Reflected a broader set of tensions: global drives towards new forms of proprietary knowledge; shifting patterns of ownership and control in the food chain; issues of corporate responsibility and corporate closeness to governments; intensifying relationships of science and scientists to the worlds of power and commerce; unease about hubristic approaches to limits in human understanding; conflicting interpretations of what might be meant by sustainable development.

Moreover, they revealed that policy frameworks for technology governance were not suitable, because they concealed socio-political agendas, resulting in a legitimacy crisis in



science, and a public distrust of regulatory institutions and science (Levidow & Marris, 2001; cf. Jasanoff, 2005). According to Kearnes and colleagues (2006: 302), “Contemporary scientific research is informed by tacit visions and imaginaries of the social role of technology” and ask for such visions to be opened up for deliberation and scrutiny in the case of nanotechnology. Xenobiology presents an opportunity as a novel technology that should not be missed, to widen the range of actors involved in the discussion about values and imaginaries that technologies embody. This is in line with Ben Hurlbut’s thinking on biocontainment, who writes: “If the technologies of the moment truly offer the power to remake life, then they might also provide occasion to revisit and rewrite our programs of governance, and so too the habits of mind and modes of imagination that underwrite them.” (Hurlbut 2017: 92).

This thesis examines how researchers in xenobiology *reimagine* life, the type of imaginaries that support such moves, and the corresponding ramifications into social and political arenas. For Sheila Jasanoff (2003), a participatory turn that gives the public a role in decision-making about technology is not sufficient. The culture of governance and mechanisms for governance need to be redeployed. In her words (p. 240), “There is a need for ‘technologies of humility’ to complement the predictive approaches: to make apparent the possibility of unforeseen consequences; to make explicit the normative that lurks within the technical; and to acknowledge from the start the need for plural viewpoints and collective learning.” Jasanoff draws attention to how problems are *framed*, as well as the active participation of individuals in risk analysis, the distribution of implications of innovation, and (most importantly for the argument of this dissertation) the learning and collective reflection from past experiences. STS researchers may find opportunities to design and carry out experimental forms of participation, as co-producers of knowledge and social order (Stilgoe & Guston, 2017).

The last theme to address, before specifying the research questions of this dissertation, concerns the politics of design in xenobiology. Langdon Winner has made us sensitive to the fact that technological artefacts have politics and embed forms of power, as they rule specific relationships between people and modes of action (Winner, 1986). He also proposed the principle that “technologies be built with a high degree of flexibility and mutability” (Winner, 1977: 326). I propose that much of the design principles involved in xenobiology not only involve forms of authority, but also embody ways of imagining responsibility and the public. Artefacts also incorporate values which must be scrutinized in depth. Other concerns for enquiry include unforeseen consequences including controllability and reversibility, as well as impacts on perceived naturalness, fairness and equity (Macnaghten & Chilvers, 2014). In this sense, I aim to address Langdon Winner's (1993) critique that the narratives of STS are

limited to suggesting that “technologies are socially constructed” (p. 373), to “call into question the basic commitments and projects of modern technological society.” (p. 375).

Following a co-productionist approach (Jasanoff, 2004c), I interrogate the emergence and stabilization of new objects in the life sciences and their political implications, in this case the intertwining of xenobiology and biocontainment. The first line of enquiry that constitutes this dissertation relates to imagination and imaginaries, of which I place emphasis on sociotechnical imaginaries (Jasanoff & Kim, 2009). Leading questions include:

- What are the values, narratives and imaginaries of xenobiology?
- What sociotechnical imaginaries lead the emergence of xenobiology? What can such imaginaries reflect about the role of scientists in society? What is their relationship to the governance of the life sciences?
- How are imaginaries related to scientific practices and expectations?
- What alternative imaginaries are possible?

By these questions I also mean what types of assumptions and ideas about life, as well as social order, are invoked by practitioners of xenobiology. This has opened enquiry in terms of how life can be reimagined (**Chapter four**), or how scientists think about the *limits* of life (Helmreich, 2008, 2011), which is tied to how they imagine the public. Interrogating imaginaries leads to matters of governance and policy, as Macnaghten, Kearnes, & Wynne (2005) write, reflecting on the role of social scientists in nanotechnology:

How do imaginaries shape trajectories of scientific research, and help define “doable” and worthwhile scientific problems? What role do they play in the allocation of funding? How do they mobilize public and private interest and opposition? And how can social science help open up such imaginaries to wider public scrutiny and debate, for the benefit of science as well as society? (ibid., p. 279).

Many individuals may see as disruptive and transgressive the profound transformations of genetic systems and our understanding of life that researchers in xenobiology may trigger, which may displace commonly held (and cherished) meanings of life. In this sense, I ask how the narratives and rhetoric of xenobiology seek to legitimize the search for limits? How do researchers aim to recruit support from other actors (i.e., government funding) to advance their research agendas? This brings us to examine ‘responsibility’ in xenobiology: Do researchers mobilize strategies to associate their field with a responsible discipline? Is the association between xenobiology and biocontainment (or safety by design) a form of responsibility?

A third stream of questions has to do with governance, in particular the framing of problems to be solved with xenobiology, aspects that are worth of deliberation, as well as who holds the authority and power to define these aspects. This brings my attention to

biocontainment and safety by design, as a form of governance by containment (Hurlbut 2017), with implications for the democratization of science.

The analysis presented in this thesis is owed to the views and thoughts that researchers shared with me, as well as my participation in conferences, workshops, and laboratory meetings. As such, I am bound to present a limited side of the story of xenobiology, while trying to be faithful to the trailblazers who aim to turn ideas about new biology into a reality. Hence, this dissertation encompasses an effort to interpret the worldview of scientists, and hopes to pave the ground for meaningful collaborations and engagements with researchers in xenobiology.

#### **1.4 Safety by design, biocontainment and xenobiology**

In this thesis I explore the motivations and justifications for research in the emerging field of xenobiology, aiming to understand how its research agenda carries social, political and ethical issues, and assumptions. As I show, xenobiology must be interpreted and understood in the light of its promise of biosafety through biocontainment, or safety-by-design (as illustrated in the storyline of Jurassic Park). Safety has become a central feature in debates about governance of technology, leaving aside other considerations of ethical and political magnitude. In multiple conversations with scientists and lay people about my research in the field, a commonly asked question was that although xenobiology sounds fascinating, but what can it accomplish? Why is research in the field being conducted? The early stages of the field implies that xenobiology is not moving in a clear or deterministic direction, making it necessary to use metaphors and promises to sustain its growth and validation. Studies in the sociology of expectations (see **Chapter two**) highlight the future-oriented nature of innovations, and the need for visions and promises to coordinate different actor communities, as well as mobilizing resources (Borup et al., 2006). Expectations and visions play a performative role, although the futures they project may not be realized (Brown & Michael, 2003). Visions and imaginaries that guide the trajectories of technology have power to determine preferred futures over others (Jasanoff, 2015a).

Xenobiology offers potential for developing novel pharmaceuticals and modes of delivery of drugs, as well as insights into how life evolved. Other applications include the development of novel (nano)materials, and platforms to evolve microorganisms efficiently (through directed evolution) (**Appendix one**). Among multiple promises I focus on the possibility of developing safe GMOs (Schmidt, 2010) by means of containment (or safety-by-design). Concern over the development of ‘safe’ GMOs has been persistent in policy and scientific circles, and still has not been fully resolved after decades of advances in genetic

engineering and legislation on the subject, related to civic epistemologies and political cultures (Jasanoff, 2005; Wright, 1994). Release of synthetic organisms, that is, their use outside the laboratory or isolated facilities such as factories,<sup>19</sup> has been identified as a major social challenge in synthetic biology (Balmer & Martin, 2008: 15). This is partly due to the conviction that the safety or hazards imposed by genetic engineering can be solved with technology, as a problem of design. For instance, the US Presidential Commission for the Study of Bioethical Issues (2010: 68)<sup>20</sup> values the possibility of *safety by design*:

Internal mechanisms to reliably contain function and reduce or eliminate these risks are being developed. “Biological isolation,” which is also termed “biosafety engineering,” aims to build in molecular “brakes” or “seatbelts” that restrain growth or replication of partially or fully synthetic organisms. Synthetic organisms can be engineered to be contained physically or temporally. Additional data are needed to assess how well biologically engineered safeguards, such as “kill switches” that activate after a defined number of generations, will work.

In **Chapter five** I explain that this bears similarities with the outcomes of the Asilomar conference in 1975 and the imaginary of governance it has maintained over decades (Hurlbut, 2015c), that both synthetic biologists and xenobiologists mobilize. Marris & Jefferson (2013) identify four considerations when addressing the importance of safety-by-design measures in synthetic biology. First, they claim that ‘built-in biocontainment’ cannot fully prevent horizontal gene transfer. Synthetic biologists recognize that “no such mechanisms could ever be infallible” (ibid, p. 22), because organisms can evolve and ‘escape’ the mechanisms designed to prevent their spread, or the transfer of genetic information intra and interspecies (horizontal gene transfer). Living systems are inherently ‘messy’, unpredictable, resistant to simple forms of control or understanding. Novel approaches like synthetic biology and systems biology aim to better understand the complexities of living systems and tame them (Calvert & Fujimura, 2011). Second, even though containment mechanisms may work to contain designed microorganisms, the genetic material (DNA) of these organisms may be present in the environment and get incorporated by other non-engineered wild species (this would not happen in xenobiology). Third, the authors note that containment mechanisms do not address external factors present in the environment, which may affect the possibility of horizontal gene transfer.<sup>21</sup> Fourth, the discourse on biosafety positions horizontal gene transfer as a hazard effect in itself, but what concerns regulators

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<sup>19</sup> Release has been defined as the lack of containment, by the Deliberate Release Directive (2001/18/EC) of the European Parliament, as “any intentional introduction into the environment of a GMO or a combination of GMOs for which no specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment.” See also Lee, 2008; Levidow & Tait, 1992.

<sup>20</sup> Commission appointed by President Barack Obama in November 2009, to study bioethical issues arising from advances in the life sciences.

<sup>21</sup> To clarify this point, the authors cite the European Decision 2002/623/EC: “the reproductive properties of the GMO itself, including the modified sequences, *the conditions of release, and particular environmental considerations such as climate (for example wind), agricultural practices, the availability of hosts for parasites*” (their emphasis).

and experts in risk assessment are the consequences or adverse effects derived from horizontal gene transfer.

In a Venn diagram (**Figure 2**) synthetic biologist Steven Benner has proposed a different view of safety in synthetic biology. He points out that the Mycobacteria with a chemically synthesized genome created by Craig Venter (Gibson et al., 2010) occupies a risky space, because it is self-sustaining, can evolve, and is made of the same biochemistry as humans. Unlike recent approaches, Benner’s synthetic biology (Benner & Sismour, 2005) aims to expand the letters of the genetic code, based on DNA, unlike recent approaches. Xenobiologists would argue that because their XNA-related materials are not found in nature xeno-organisms would not be self-sustaining, providing an additional layer of safety. In **Chapter four** I address in detail the sociotechnical imaginary of control over nature that justifies the rationale that in xenobiology, the unnatural is safer than the natural. Creating the narrative that real hazards are brought by DNA-based organisms, and XNA-based organisms constitute a “safe space for experimentation” (Schmidt, 2010) puts forward a set of questions about responsibility and the nature of limits that xenobiology aims to challenge.

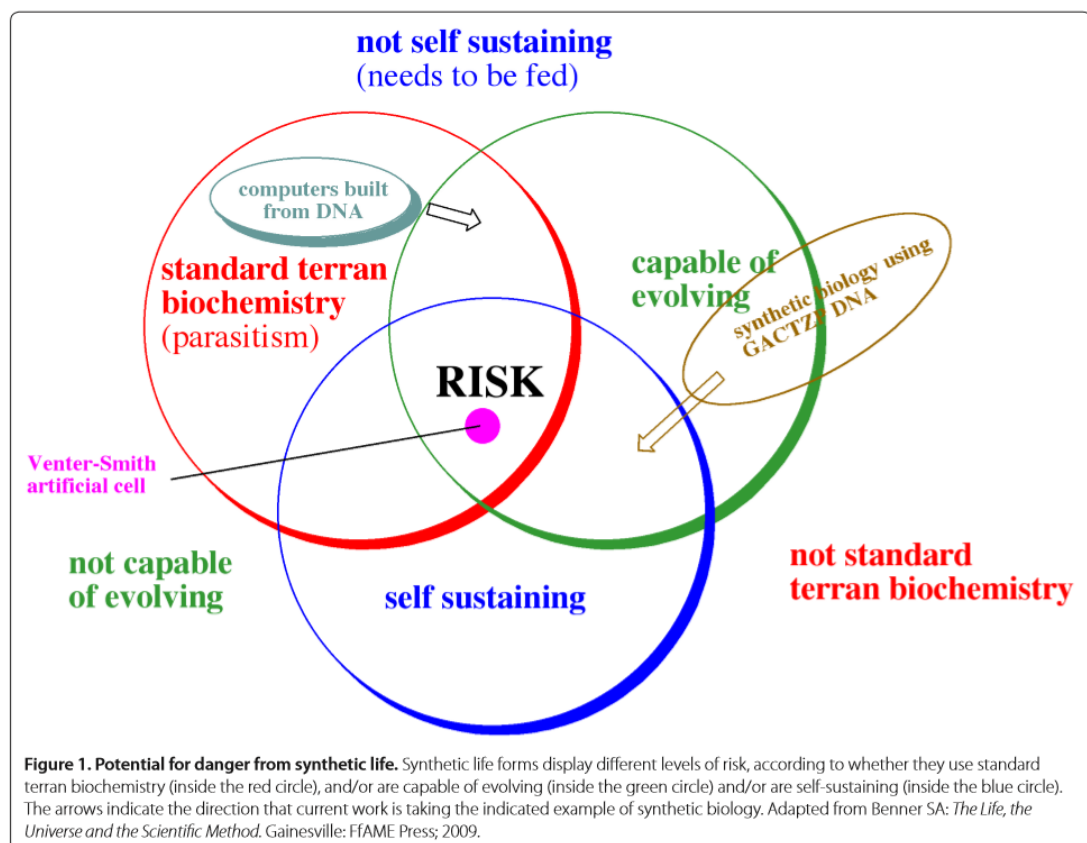


Figure 2. Potential for danger from synthetic life according to Steven Benner (Benner, 2010: 3).

Xenobiology looks like a *Janus head*, with one head facing fundamental questions about the origin of life and the core elements of biology, and on the other head, applications of

interest for the bioeconomy, like biomedicines or even nanomaterials (i.e. Pinheiro & Holliger, 2014; Taylor et al., 2016). The release of microorganisms into the environment enabled (or legitimized) by xenobiology and its promise of safety, complicate the picture further. Release has been defined by the Deliberate Release Directive (2001/18/EC) of the European Commission as “any intentional introduction into the environment of a GMO or a combination of GMOs for which no specific containment measures are used to limit their contact with, and to provide a high level of safety for, the general population and the environment.” (cf. Lee, 2008; Levidow & Tait, 1992). The use of genetically modified microorganisms has been restricted to laboratories or physically contained settings, such as bioreactors in factories. The EU Directive 2009/41/EC on the contained use of genetically modified micro-organisms imposes restrictions on the use of genetically modified microorganisms in open environments anywhere beyond the walls of a laboratory (cf. Hamlyn, 2018; Lee, 2008). The possibility of releasing genetically modified micro-organisms in the environment should not be taken lightly. As Marris & Jefferson (2013: 10) explain, this has been addressed previously:

25 years on, hardly any commercial products consisting of a GMMO [Genetically modified microorganism] that requires deliberate release into the environment to perform its intended function have entered the EU or US market, very few experimental releases are currently being conducted, and firms seem reluctant to invest in this area.

An example of GMO use in open environments is the *Arsenic Biosensor*<sup>22</sup> developed by researchers from the University of Cambridge. The biosensor consists of a recipient that contains bacteria capable of changing colour if the concentration of arsenic in a sample is higher than an established threshold, therefore allowing the detection of arsenic contamination in water for drinking purposes; this was developed for rural villages in Nepal. However, the project encountered regulatory obstacles that have not made possible its implementation in the communities it was supposed to benefit.<sup>23</sup> Another avenue concerns the development of microorganisms that can remediate (degrade, or digest) hazardous environmental chemicals (Pieper & Reineke, 2000), including plastics, or oil spills. Among the chemicals that can be degraded is the herbicide atrazine (Sinha et al., 2010).

Proponents of xenobiology framed the field as capable of producing ‘safe organisms’, which cannot proliferate if not given xenobiotics (or synthetic nutrients) and cannot transmit their genetic material to other organisms. In this regard, Farren Isaacs (corresponding author of Rovner et al., 2015), a synthetic biologist whose research has been crucial for xenobiology, commented for an article by science writer Elie Dolgin (2015: 423) in *Nature*: “Establishing

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<sup>22</sup> See <http://arsenicbiosensor.org/> [last visited October 13, 2017].

<sup>23</sup> Sundaram, L. (2017, May). Beyond Product or Process: The Role of Context in Regulating Genetically-Modified Organisms. Paper presented at the Fifth Annual Conference on Governance of Emerging Technologies: Law, Policy and Ethics, Phoenix.

safety and security from the get-go will really enable broad and open use of engineered organisms.” The projected possibilities of employing GMOs in open environments open the question of engineering not only organisms but microbial communities (Scott et al., 2017), which necessarily invokes the imagination of large scale ecosystem engineering, or what scientists call ‘terraforming’; and why not consider the possibility of modifying the atmosphere and living conditions in other planets.<sup>24</sup> Interviewees explained that synthetic biology at this point is far from fulfilling this possibility. According to de Lorenzo and colleagues (2016: 623), what is at stake is that “[c]ontemporary SynBio allows for the first time in the Earth’s history not only [to] *invent* biological activities which have not been available before in nature, but also *their deliberate* spreading through much larger, even global-scale ecosystems” (emphasis original). The deliberate spread of microorganisms in the environment is meant to cross an imagined barrier, made solid by means of regulation between the laboratory and society. The applications I mentioned above that require the release of microorganisms into the environment are not obviously related with the goals of xenobiology, like expanding the genetic code or producing proteins with non-natural amino-acids. When researchers make the connection between a research field and possible applications, they determine what problems are worth doing and what tools can be recruited to solve them. The perceived possibility for xenobiology to allow microorganisms to step out of the laboratory into the “real world” serves to justify research in the field and open frontiers of life and science within society.

Ben Hurlbut (2017) refers to “governance-by-containment” as a vision and framework of governance, regardless of the technical feasibility of containment mechanisms in genetically modified organisms. He highlights its “revolution-risk asymmetry”, the assumption that the social benefits of biotechnology are unlimited, and taken for granted, whereas the risks that derive from it must be demonstrated and can be manageable with engineering principles. This works insofar containment is invoked, because if risks are controllable, there is no justification to deny the benefits of new technologies. In Hurlbut’s words, the “corollary to the promise that risk can be contained is the promise of an endless frontier of technological progress” (ibid, p. 86).

The limits in xenobiology are also limits of society and nature. As Pasteur was successful in bringing the real world into the laboratory and back to society (Latour, 1988b), now xenobiologists aim to take their modified organisms out of the laboratory and have them carry out applications that are currently not possible, or difficult to obtain permission for.

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<sup>24</sup> See Dy, A. 2017. Synthetic biology to help colonize Mars. Blog ‘Plos SynBio Community.’ <http://blogs.plos.org/synbio/2017/03/01/synthetic-biology-to-help-colonize-mars/> [last visited October 13, 2017].

Xenobiology thus aims to redefine the boundaries of the biological world, and the boundaries of society in the laboratory. The problem is that such renegotiations of boundaries are packaged as a technical question, drawing out most of the attention on ethical and political issues in the field. The insightful analysis of Hurlbut (2017) suggests that imagining risks as problems of containment, restricts participation of the public and the range of moral and political questions that can be asked. Ben Hurlbut (2015) has explained how the Asilomar conference produced a sociotechnical imaginary of governance (Asilomar-in-memory), in which the public was excluded from decisions and (parts of society) seen as a risk for the development of technology, in a linear model of progress. Additionally, scientists are expected to self-govern themselves, anticipate risks of technologies, and display the appropriate reasoning over what is the best course of a technology. A focus on biocontainment distracts and impairs deliberation on how to govern emerging technologies. Establishing a divide between the laboratory and society is no longer tenable in the context of emerging technologies and inhibits the type of learning and collective experimentation that is required for areas such as xenobiology, in which risks cannot be defined (and uncertainty must be embraced), and greater public involvement should be present. Research cannot be ‘kept within a lab,’ as if it was not part of the world already. If we are to take seriously the idea behind xenobiology, of pushing the limits of what life can be, we should not be concerned whether this is encapsulated in a laboratory, in society, or in the environment. In other words, these categories cannot be separated.

### 1.5 Final remarks and outline

STS commentators have turned their attention to synthetic biology because it offers a new subject of study where new institutions, aspirations, and implications coalesce (**Chapter two**). Synthetic biology offers an opportunity to address governance issues from an early beginning, providing a valuable opportunity for social scientists to influence the trajectory of a field. Similarly to nanotechnology, synthetic biology offers a valuable opportunity to earn public trust and acceptance from early stages, by integrating social and ethical aspects with research in the laboratory (Fisher & Mahajan, 2006a). Xenobiology taps into previous controversies on biosafety concerning the large-scale damage to ecosystems and human health and not as much into biosecurity, in which concern is on biological agents that could be intentionally misused (cf. Garfinkle & Knowles, 2014). One major concern in policy circles is the acceptability of synthetic biology (Marris & Calvert, 2019). In this thesis I illustrate that biosafety concerns are recruited by promoters of xenobiology to legitimize the field, and used as an *opportunity* to expand biotechnology to open environments.



The structure of this dissertation is as follows. **Chapter two** offers an overview of theoretical insights from Science and Technology Studies that inform the analysis presented in this thesis. I refer to the idiom of ‘co-production’ (Jasanoff 2004) to understand the commitments of xenobiology as a scientific discipline that captures understandings of the relationship between science and the public. This is supported by a discussion of the literature on imaginaries, including sociotechnical imaginaries (Jasanoff & Kim 2009), technobiological imaginaries (Fujimura, 2011), technoscientific imaginaries (Marcus, 1995), and sociotechnical vanguards (Hilgartner, 2015). These concepts will be useful for the goal of examining what narratives, imaginaries and visions lead the development of xenobiology. A third stream of literature concerns the sociology of risk, along with “collective experimentation” (Latour, 2004) and “real-world experimentation” (Krohn & Weyer, 1994), because society itself is an ongoing experiment, and scientific research inherently involves all citizens. It is useful to think about the control and uncertainty that are at stake in xenobiology and biocontainment. The rest of the chapter addresses other important areas of governance of technology and STS, including sociology of expectations, and public understanding of science.

**Chapter three** explains the methods (and the rationale for their choice) I used to study xenobiology as a field in the making. The research approach for this thesis was qualitative, based around thirty-four interviews with synthetic biologists comprised of doctoral students, postdoctoral researchers, and professors. This was supported by twelve-months of participant observation in a xenobiology laboratory. In addition to conducting fieldwork in the laboratory, I organized five discussions with members of the laboratory, addressing social and political aspects of xenobiology.

**Chapter four** considers xenobiology as a way of thinking about life as being unlimited. I examine the rhetoric that the unnatural is the safer option, and scientists aim to challenge the limits of what is biologically possible. In this section I elaborate on what I call the sociotechnical imaginary of ‘life unbound,’ the premise that life does not need to be based on DNA, nor tied to an evolutionary history. Some researchers like Philippe Marlière frame such exploration with narratives and metaphors of navigation of exploration, meant to create a niche that only xenobiology can occupy, which is also a safe space, to fulfil a promise of safety-by-design in biotechnology. Nevertheless, concern over limits raises a number of questions about responsibility, as one of the researchers I interviewed expressed, ‘Where do we draw the line?’

**Chapter five** looks at biocontainment as a form of governance by design, which as a legacy of the Asilomar conference, encapsulates a form of imagining risks that can be managed via technical solutions found in the laboratory. This form of imagination about

technological design that prioritizes risks, incorporates (or negates) democratic principles as it narrows down the scope for deliberation and provides an illusion of control. I introduce what I call the sociotechnical imaginary of ‘controllable emergence,’ which assumes that controlling biological systems can ensure control over public acceptance.

**Chapter six** continues the discussion on governance by biocontainment and the sociotechnical imaginary of controllable emergence, in accordance to the notion that limits are also social that I present in this dissertation. I turn the focus of the analysis toward how scientists respond to the needs of the public perceived as fearful of new technologies, constructing a discourse of biosafety that is not a settled scientific dispute. In the second half of the chapter, I show that xenobiologists associate responsibility with control of organisms, delineating responsible practices to the type of experiments and results that are produced in the laboratory.

In **Chapter seven**, the last chapter that analyses empirical data, takes distance from the study of imaginaries and relations between scientists and the public, to suggest that that the approach of xenobiology to biology is reductionist, in part given the materiality of the field and the focus on interventions at the level of the individual. I bring attention to the need to think about wider ramifications of xenobiology, including environmental toxicity. I refer to discussions on the subject with the laboratory where I studied, and identify barriers for thinking about the ramifications of xenobiology in systemic ways. I make the case for embracing frameworks of governance that include real-world experimentation and adaptive governance that embrace uncertainty and decrease the illusion of control and safety.

**Chapter eight** gathers the main points I aim to illustrate, providing an overview of the main arguments I make in each chapter, relating them to the literature on STS and the governance of technology, and emphasizing their contribution for theory-building. I divide such contributions in two aspects: the notion of responsibility in scientific practice; and the role of imagination and imaginaries in framing and constituting visions of the future attainable through technology. I finish this thesis by suggesting further avenues for research and refined methodological considerations.

In **Appendix one**, I provide an overview of scientific achievements in xenobiology, signalling the most important developments in the field, which traces its roots to the dawn of molecular biology. Subsequently, this chapter expands on the possibilities, or potential applications of xenobiology. I point out the tensions of xenobiology between being a fundamental and an applied science (understanding that these categories are not discrete and overlap). It is in this landscape that biocontainment and the ‘release’ of genetically modified microorganisms to the environment should be considered.

## 2. Literature review

In this thesis I argue that imagination influences how scientists conduct their research agendas and determine what is accomplishable in the laboratory. Imagination and the imaginaries that sustain the progress of a field, invoke not only technical aspects, but assumptions and values about what is possible in biology, and how societies may receive or react to new advances. As xenobiologists aim to capitalize on a discourse of control over life and society, I suggest drawing on governance frameworks that recognize the importance of uncertainty and adaptability in new situations. Hence, technology development, as a social experiment, requires new ways of thinking and deploying experiments and field tests that involve the public and take into account issues that are subject of deliberation beyond matters of risk. Among the few scholars that have paid attention to xenobiology is the philosopher of science Bernadette Bensaude Vincent (2013: 373), who claims that:

The mode of existence of the objects designed in synthetic biology laboratories at the borderline between the natural and the artificial, between the living and the non-living, inevitably questions the grand divides that are the backbones of modern Western culture. They raise issues about the place and role of humans in nature, their relations to animal life, and to the environment in general.

Yet, xenobiology raises questions about how scientists perceive the public, and exert forms of authority in determining what issues are at stake, and what can be understood as responsibility in science. The field also offers an opportunity to understand the dynamics of emerging technologies, in particular how visions and imaginaries that vanguards promote become institutionalized and adopted by larger collectives.

The constructivist approach of STS is useful for this thesis because it targets the constructed and contested nature of categories like xenobiology, biosafety, biocontainment, and puts into question the interests and efforts of scientists to legitimize research in the field. This aim is well suited by the literature in STS. Alan Irwin (2008: 600) makes a call for ensuring that “STS research is not marginalized as “interesting qualitative work” (or as bringing “colour” to the “black and white” representations of macro social science)”, and xenobiology offers a window of opportunity to engage with scientists and publics over how technologies reconfigure social fabrics and bring into being novel futures.

STS has roots in the Sociology of Scientific Knowledge (SSK) that has examined technoscientific controversies and how they come to closure (Bloor, 1976; Collins, 1985). SSK takes a symmetrical approach to both sides of a controversy to explain both truth and falsity using the same resources (Bloor 1976). For example, the reasons why we come to

believe DNA has a double helix structure are more than the fact that DNA is a double helix, there is a social context in which the decisions that led to the discovery were made. The type of explanations for the success of a scientific theory must be the same for the failure of a theory, in this way, scientific knowledge is not privileged because it aspires to truth. SSK has been criticized for not being reflexive about its source of cognitive authority, among other concerns (Sismondo, 2004: 52). Another approximation criticizes the social realist stance of SSK, which lies in the social side of a spectrum composed by nature and social explanations in its extremes (Callon & Latour, 1992). These authors note that the distinction between social and nature is a consequence of scientists' world view that Harry Collins criticizes. SSK also became embroiled in a debate over commitment versus neutrality, which poses the question of how much scholars should commit politically with respect to the controversies they study. Scott, Richards, & Martin (1990) argued that SSK scholars cannot avoid being drawn politically into the controversies they study, and usually are co-opted by the weaker side. The debate was recollected in a 1996 issue of *Social Studies of Science*, in which Ashmore (1996) defends SSK by arguing that it is not possible to choose sides, since only when controversies are resolved it is determined who won and who lost. Collins (1996) added that symmetry and neutrality are useful aims to which scholars should aspire, and important as methodological approach. For Malcolm Ashmore (1996), however, symmetry is an epistemological commitment, not a methodological tool. In the same issue of *Social Studies of Science*, Brian Wynne (1996) argues that SSK ignores that controversies take place within society and clarifies that the controversies that Collins has studied had taken place within science, not involving the public. Sheila Jasanoff (1996) complements this perspective by arguing that SSK focuses on sides and controversies, failing to acknowledge the complexity of society, in which science plays a central role. For Jasanoff, the production of knowledge is political, and SSK scholars should consider how their research can be used for political purposes (such as deconstructing scientific arguments by multinational corporations to support tobacco in court), as well as how their choice of research context, or controversy, has political and social implications.

This chapter sets out the current limits of our understanding of how emerging technologies shape society as they unfold, and how they are transformed based on assumptions about the needs of society. I begin this chapter by providing an overview of sociological and STS studies about synthetic biology, since this discipline is the closest 'relative' of xenobiology. Few studies have addressed the social, ethical and political aspects of xenobiology and its relationship with biosafety. In the second section I review the literature on the concept of co-production and co-evolutionary approaches to science and society. Studies in this regard reinforce questioning power and politics in science and technology. Next, in the third section, I turn to conceptualizations on social imaginaries,

expanding on concepts like sociotechnical imaginaries, technoscientific imaginaries, and technobiological imaginaries. As these concepts share a concern about how science shapes the future, I also introduce themes in sociology of expectations. Related to imagination, I provide an overview of how scientists imagine and construct publics. In the fourth section I introduce the concepts of real-world experimentation and ‘collective experimentation’, which question the barriers between laboratory and society, view experimentation as a social endeavour since experimentation and new technologies inevitable affect (positively or negatively) larger collectives than the laboratory. I finish this chapter by providing an overview of experimentation in terms of addressing ethical, political and social aspects of emerging technologies with scientists, in an effort to promote reflexivity about the power of technology to reconfigure society and build new worlds.

In this chapter I provide an overview of theoretical insights from Science and Technology Studies (STS) and governance of technology that inform the analysis presented in this thesis. First, I explain the main questions that scholars of social studies in synthetic biology have tackled, in order to provide context for the questions I ask about xenobiology. In the second part of the chapter, **section 2.2**, I present the main works in STS related to the idiom of co-production (Jasanoff 2004) because this group of theoretical constructs help to conceptualize xenobiology as a scientific discipline situated in particular social order. Then I turn in **section 2.3** to the literature from STS, political science and anthropology that concerns the future as subject of analysis. In the third **section (2.4)**, I present insights from sociology of risk, along with collective experimentation (Latour, 2004) and ‘real-world experimentation’ (Krohn & Weyer, 1994), frameworks for thinking about risk that are useful when considering control and uncertainty in xenobiology and biocontainment. In **section 2.5** I present works in ethics of science and technology, focused on the efforts of social scientists to integrate with scientists in the laboratory to widen the spectrum of questions asked in scientific enterprises. The studies I present will be useful for the understanding of the analysis of imaginaries and narratives in xenobiology, and the mechanisms of governance that biocontainment encapsulates, including particular forms of representing perceptions about the public and the framing of problems in biotechnology.

## **2.1 Social studies on synthetic biology**

STS commentators have turned their attention during the last decade to synthetic biology, because it has offered a new subject of study where new institutions, aspirations, and implications coalesce. In what follows, I provide an overview of important works in the STS literature on synthetic biology to provide context on the type of questions that scholars have

asked. This is important to situate the questions I place about xenobiology, with an eye on whether advances in xenobiology raise new questions or challenges. The goal of synthesizing life has been a recurring idea throughout the history of biology (Campos, 2009). Commentators have given attention to the attempts of synthetic biologists to imagine and make biology an engineering discipline (Andrianantoandro et al., 2006; Brent, 2004; Endy, 2005), and to the challenges this presents both epistemically and materially.<sup>25</sup> Different streams of synthetic biology, including xenobiology, protocell research, and making synthetic biology an engineering discipline, share a common interest in mastering control over biology. In this section I focus mostly on the so-called ‘parts-based’ synthetic biology (cf. O’Malley et al., 2008)<sup>26</sup> because this approach has received most attention from social scientists. In contrast, xenobiology or ‘orthogonal biology’ have not received much attention, a gap that this thesis aims to fill. Emma Frow (2013: 433) characterizes the parts-based approach as follows:

Parts-based synthetic biology advances an imagination of DNA as text or code that can be composed and (re-)written for instrumental ends. Rather than simply studying, mapping or representing biological processes, practitioners are explicitly application-oriented and focus on creating new living entities for useful purposes. Furthermore, they are concerned with creating life that performs according to certain metrics or rules; *life in which complexity and emergence can be managed, and in which evolution is brought under control*. As a means to this end, they propose breaking down the genomes of living organisms into component ‘parts’ associated with defined functions (emphasis added).

Studies of synthetic biology as a community have attempted to understand its consolidation as a scientific discipline. Naming a discipline encompasses the articulation of specific problems that do not fall within other disciplines, methodologies, or technologies. The recognition earned attracts support from funders and consolidates a sense of community (Powell et al., 2007). That synthetic biology has earned itself a name and popular position in the life sciences is noteworthy; the names of disciplines have performative power and can be open to different definitions where having flexible boundaries may account for the success of a name. Naming an emerging technology can also be a rhetorical strategy (Hedgecoe, 2003; van Lente & Rip, 1998). The epistemic heterogeneity of synthetic biology has allowed the field to reach diverse audiences and hence achieve stabilization (Raimbault, Cointet, & Joly, 2016).

Molyneux-Hodgson & Meyer (2009) studied the emergence of synthetic biology as a scientific community. They identified four tales of emergence that account for the story of synthetic biology. For them, the origins of synthetic biology are the result of policy efforts in the EU and the UK, and local networks. They refer to the devices that help to build a

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<sup>25</sup> See Kwok (2010) for an overview of technical challenges in synthetic biology, including unpredictability and complexity.

<sup>26</sup> On the history of synthetic biology see Luisi, 2006; Peretó, 2016; Peretó & Català, 2007.

community, which include policy initiatives, workshops, calls for proposals and networks, as community-making devices. The process of discipline building, in addition to practices and institutions, is influenced by values and visions.<sup>27</sup> Bernadette Bensaude Vincent (2013b) contrasts two visions of synthetic biology, one of Drew Endy (2005), and the other of Steven Benner (i.e., Benner & Sismour (2005), showing differences in their agendas, their relations to the past (for example, as a continuation or breakage from organic chemistry), their visions of the future, and their relation to intellectual property and openness. Competing visions of synthetic biology can coexist, and in a form of epistemic pluralism the fields will never achieve a unique disciplinary status.

The kind of social institutions and community building efforts that have been put in place to consolidate and give cohesion to synthetic biology has attracted the social study of synthetic biology. Among these institutions are the International Genetically Engineered Machine (iGEM) foundation,<sup>28</sup> and the Registry of Standard Parts, which coordinates the exchange and curation of BioBricks; BioBricks are expected to be used interchangeably as ‘Lego’ blocks, enabling fast and streamlined design of biological systems. BioBricks are meant to form the basis for the engineering of systems, serving as ready to use and mix components, in a similar way that electrical engineers use resistors and standard capacitors, or computer programmers use modular blocks of code. The idea behind the Registry of Standard Parts is that biological parts can be combined in different ways to produce different types of biological devices and systems. Leaving aside the biological feasibility of BioBricks, they are coordinated by the BioBricks Foundation (BBF), a non-profit organisation established to ensure that the parts produced for the registry remain freely available to the public. This has been referred to as a synthetic biology “commons,” although it faces difficulties in adopting copyright backing and patents available in the public domain (Rai & Boyle, 2007).

The iGEM competition has provided a fertile ground for the social studies of synthetic biology as a community-building effort. It has been studied as a form of social engineering that trains and indoctrinates the next generation of synthetic biologists (Cockerton, 2011). The composition of iGEM serves to reinforce certain values and dispositions through the prize system. For instance, when awarding gold medals (the top prize), the judging system

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<sup>27</sup> For discipline building, or formation of new disciplines, see Barry, Born, & Weszkalnys, 2008; Leonelli & Ankeny, 2015.

<sup>28</sup> iGEM started in MIT in 2003 by a group of computer scientists and engineers as an undergraduate course that over the years expanded to a worldwide undergraduate Synthetic Biology competition, with 369 teams registered for the 2018 contest. Working during the summer in their schools, students are given a kit of biological parts (named BioBricks), which perform biological functions in a modular manner— from the Registry of Standard Biological Parts. Students are expected to use and design new parts which are then given back to the Registry. See [http://igem.org/IGEM/Learn\\_About](http://igem.org/IGEM/Learn_About), and [http://igem.org/Team\\_List](http://igem.org/Team_List) [last visited June 26, 2018].

gives preferences to studies about perceptions of risk as biosafety or biosecurity in the laboratory, rather than the contestation of values and social arrangements. In this sense, Evans & Frow (2015) ask what framings are absent when “dual use” and security are seen as what needs to be taken care of. Nevertheless, the ‘policy and practices’ component of iGEM, which supports social and ethical companion to the scientific projects,<sup>29</sup> can offer a space for Responsible Research and Innovation, for example the exploration of “techno-moral scenarios” and ways in which synthetic biology shapes the future (Stemerding, 2015).

Studying iGEM as a space to explore the complicated relationship between the rhetoric of biology and engineering in the constitution of synthetic biology, Frow & Calvert (2013) note the tensions and difficulties that arise from integrating engineering with biology. To overcome tensions, they argue, students redefine values, practices and ways of knowing, giving rise to a moral economy that “capture[s] the fluidity in epistemic and institutional systems that currently characterize iGEM more aptly than focusing on the more reified concept of epistemic cultures” (ibid., p. 55). Other studies have analysed practices of valuation of BioBricks and how value is constituted in synthetic biology (Frow, 2013). Nevertheless, the competition also has lent itself to experimentation in forms of collaboration with social scientists, part of the ‘policy and practice’ component (formerly ‘human practices’). Balmer & Bulpin (2013) developed what they call ‘sociotechnical circuits’ (a form of ethical *equipment*, following Rabinow & Bennett (2012) which depict the roles and relations of the team as an electronic circuit inspired in the modular approach of synthetic biology as a tool for promoting reflection on the members of the team about their roles and choices.

For synthetic biologists, previous efforts in genetic engineering and biotechnology were very distant from a controlled manipulation of the constituents of living organisms. Synthetic biology presents a new way of approaching biology. O’Malley and colleagues (2008) identified differences at the epistemological, methodological and intellectual property levels, of three categories of synthetic biology: DNA-based device construction, genome-driven cell engineering, and protocell creation. Attempts at reducing the field’s complexity based on ‘knowing-as-making,’ go against traditional efforts of understanding biological systems as complex self-organizing entities. O’Malley (2009) reflects further on the relationship between synthetic biology and ‘knowledge making,’ arguing that *kludging*, a colloquial term for referring to making the system work, rather than expressing concern over the knowledge behind process to get there, is a process found in most fields of biology. But synthetic biology

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<sup>29</sup> In the iGEM competition, one of the track that judges evaluate is the assessment of the projects that students present in terms of risk, law and regulation, ethics, public engagement, sustainability, and philosophical aspects; cf. [http://2017.igem.org/Human\\_Practices](http://2017.igem.org/Human_Practices) [last visited September 23, 2018].



bears a tension of wanting to avoid kludging in its desire to make nature elegant and efficient according to engineering principles and using it as highly creative force.

Studies of epistemic practices have contrasted knowledge making in engineering and synthetic biology. Comparing aeronautics with synthetic biology, Schyfter (2013) argues that engineering knowledge centres around making artefacts, which gives engineering its own epistemic tradition and disciplinary status. While synthetic biology shares this orientation toward making artefacts, making knowledge also serves to build a community and a discipline based on engineering knowledge. However, synthetic biology does not fit precisely in traditional engineering practices, as synthetic biology artefacts occupy an undefined space between technological objects and natural kinds (Schyfter, 2011). Calvert (2013) studied the contested epistemological aspirations of synthetic biology, finding that the project of synthetic of biology not only consists of applying engineering principles to biology, but also carries non-technical components including social arrangements and institutions, such as openness, safety and sharing. Moreover, the engineering approach to biology has led to a negotiation of practices and meanings to differentiate the field from molecular biology, in which engineers and biologists adjust their work to make it possible to work with other disciplines (Finlay, 2013).

A major question is how synthesis can lead to the production of specific knowledge in biology.<sup>30</sup> Different configurations of synthetic biology in the last century have shared a complex relationship between knowing (understanding, representing) and making (constructing, intervening), but the emphasis of synthetic biology is to engineer novel organisms (Keller, 2009). For Keller, it is not clear how much synthetic biology has contributed to a better understanding of biology. Nevertheless, synthesis and analysis can coexist, Malaterre (2013) argues, suggesting a distinction between two types of knowledge that are relevant for synthetic biology: 'knowledge-how' (how to intervene or manipulate nature) and 'knowledge-why.' For him, successful synthesis leads to 'know-how', which can lead to 'knowledge-why.'

Social analysts have also placed attention to a close cousin of synthetic biology, systems biology, a field that studies complex interactions within biological systems using a holistic approach. It has been studied in terms of its epistemic aspirations and commitments of systems biology that distinguish it from earlier reductionist approaches like molecular biology (Calvert & Fujimura, 2011), and its techno-epistemic cultures and visions

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<sup>30</sup> For a practitioner's perspective, see Benner (2013), who argues in favor of synthesis as a way of knowing, particularly relevant for his studies of DNA that gained insights from unnatural base pairs which conventional methods did not offer.

(Kastenhofer, 2013). Jane Calvert (2013b) has studied the policy narratives of progress in biotechnology, with systems biology as *big science*.

In their study of synthetic biology, social scientists have forged strong links with synthetic biologists. This has resulted in framing the discipline as interdisciplinary and ‘in the making’, following calls to promote closer integration between emerging technologies, such as nanotechnology, artificial intelligence, geoengineering, synthetic biology and social science, building upon previous ELSI/ELSA efforts (cf. Fisher, 2005). Collaborations have sought to reframe the role of the social scientist in knowledge production and meaning (Calvert & Martin, 2009). Social scientists have mediated spaces for collaboration between scientists, designers and artists (Ginsberg et al., 2014). Such forms of collaboration have the potential to bring novel forms of critique in STS, encouraging open-ended perspectives in an experimental manner, without knowing from the start what the outcome of the collaboration will be (Calvert & Schyfter, 2017). Interest in bringing together art and design have led to the incorporation in the iGEM competition of the art and design track.<sup>31</sup> Other examples include *The Art of Antibiotics: Two Residencies. Two Artists. Two Labs* (Schmidt, 2018), that aims to raise awareness about antimicrobial resistance worldwide.

In *Synthetic Aesthetics* (Ginsberg et al., 2014), six collaborations or ‘residences’ were established by social scientists between a synthetic biologist and an artist/designer. Projects were far ranging, from making cheese using bacteria collected from human body parts – addressing the notion that we are what we eat, to exploring geological timescales with cyanobacteria deposit minerals. At the heart of the projects was an interrogation of the relation between design and synthetic biology, moving beyond one-dimensional limitations of disciplines, generating new avenues of reflection, and challenging existing visions. Among the residences was the collaboration between biochemist Sheref Mansy and artist/designer Sascha Pohflepp. They explored theoretically the transition from the non-living to the living, and what separates machines from living beings. They consider non-living machines as a short transition in the exploitation by humans of modes of energy transformation by humans, which started with the domestication of animals and will continue into the not-so-distant future of synthetic living organisms (Mansy & Pohflepp, 2014). Although inspired in evolutionary experiments that aim to recreate selective pressures in a laboratory, they did not engage in experimenting with objects or matter. Commenting on the work of Mansy and Pohflepp, Jane Calvert (2014) discusses other relevant aspects of the relation between evolution and design, as synthetic biology seeks to incorporate engineering principles which historically bore no possibility of incorporating evolutionary qualities. Moreover, she

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<sup>31</sup> See [http://2017.igem.org/Competition/Tracks/Art\\_Design](http://2017.igem.org/Competition/Tracks/Art_Design) [Last visited June 29, 2018].

addressed the relation between design and ‘directed evolution’, an approach paramount to the development of xenobiology.<sup>32</sup>

Last, the emergence and diffusion of synthetic biology raises biosafety and biosecurity concerns,<sup>33</sup> according to (Schmidt, 2008), due to the expansion of the range of actors with access to biotechnology and its simplicity to use, such as biohackers, expanded funding and biodefence research efforts in the US, and accidents in contained biosafe laboratories<sup>34</sup>. Indeed, the promise of synthetic biology of making biology easier to engineer has been associated with ‘de-skilling,’ raising fears that the entry barrier to conduct experimentation in biology is reduced; in other words, making it easier for untrained people to work with biotechnology. Instead of pointing out possible threats occasioned by the extended access to biotechnology that synthetic biology offers, Bennett and colleagues (2009) challenge technical approaches like safety-by-design and screening technologies to govern synthetic biology, “such that the ‘bad guys’ can’t reengineer what the ‘good-guys’ have made” (ibid., p. 1110). They agree with Schmidt and others that the entrance of new actors (like DIY-bio) may bring unanticipated risks, but rather point out the need for new analytic and policy frameworks, including “human practices” (Rabinow & Bennett, 2012), that shift attention from the technical to the practices of those involved in taking synthetic biology from promises and imagination to reality.

Concerns over biosecurity have been linked to the potential development of biological warfare, including the creation or modification of existing viruses through commercial DNA synthesis. The biosecurity risks have sparked discussions about how to govern and regulate the field, which raises uncertainties about norms and regulatory controls, and the need for adaptive responses (Mukunda, Oye, & Mohr, 2009; Zhang, Marris, & Rose, 2011). Sam Weiss Evans (2015) asks about the meaning of governing security concerns that are not yet known, redirecting attention to what are considered the subjects and objects of security control. Most of the discussion around biosecurity has centred around an imagination of threats and risks based on different interpretations of previous efforts in biological warfare and misuse. Based on Rayner's (2012) concept of “unknown knowns,” Marris, Jefferson, & Lentzos (2014) show that framings of dual use and their respective policy responses are dysfunctional, or *misplaced*: the underestimation of the possible threats of synthetic biology

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<sup>32</sup> The research agenda of xenobiology (with the creation of XNAs, polymerases and other components of a genetic system) is based on this form selection, which by definition incorporates features not knowable.

<sup>33</sup> For background on biosafety and biosecurity in synthetic biology, see also: Garfinkle & Knowles, 2014; Jefferson, Lentzos, & Marris, 2014b; National Academies of Sciences Engineering and Medicine, 2018; National Science Advisory Board for Biosecurity, 2006; Presidential Commission for the Study of Bioethical Issues, 2010. For governance challenges of biosafety in biotechnology, see Gupta, 2013.

<sup>34</sup> For instance, laboratories with Biosafety levels 3 and 4, in which dangerous pathogens such as Anthrax are handled; cf. Trevan (2015).

serves to maintain the promises of benefits that the field has made, hence constructing knowledge and ignorance serve the goals of the field.

In summary, the social study of synthetic biology has been fruitful for understanding the formation of scientific communities and new ethos and regimes that disciplines adopt. Synthetic biology as an emerging discipline, has been caught on debates about the role and consequences of new technologies in society, and similar to nanotechnology or geoengineering, have been seen as opportunities to earn public trust; in this regard, xenobiology faces similar challenges and opportunities. Synthetic biology has also provided a space of integration with social scientists, who have addressed the difficulties of collaborating with natural scientists and breaking a decades-long moral division of labour, a theme to which I aim to contribute in this thesis. Nevertheless, rather than engaging with xenobiology as a community, I aim to derive lessons for thinking about responsibility in science, and how researchers think about life in order to draw lessons for emerging biotechnologies of the twenty-first century. As xenobiology unfolds, I study whether responsibility is part of its ethos, and the elements that are involved when thinking about responsibility in a more comprehensive way.

## **2.2 Co-production and co-evolutionary perspectives of science and society**

### **2.2.1 Co-production: science and society and representation**

STS scholars aim to challenge frameworks in the study of technology that consider technology trajectories as deterministic or isolated from social influence. In recognizing the importance of social factors, this leads to the intuitive notion that science and society influence each other. In the introductory chapter of his edited book, *A Sociology of Monsters*, John Law (1991) claims that STS aims to look at the social and technical together, of which sociotechnical systems are a feature; for Law, the ‘monsters’ are about heterogeneity. In what follows, I provide an overview of uses of the term co-production and similar approximations, like co-evolution and co-construction. Xenobiology itself combines and challenges different cultural categorizations, such as life and the synthetic, safety and risk, scientists and society, and control and uncertainty. The framing and aspirations of the field need to be understood in a particular cultural moment, reflecting tensions about the role of science in democratic society, and the solutions (and its justification) that research in the life sciences can provide.

Schot & Rip (1997) refer to co-production in the context of “constructive technology assessment” (cf. Rip, Misa, & Schot, 1995), a governance framework that embraces participation in early stages of a technology’s development, which they conceptualize as an attempt to “achieving better technologies (in a better society)” (ibid., p. 6). Recognizing

technology development as a social enterprise, the impacts of technology are understood as owing to its technological power and the actions of governments, unions or pressure groups. These authors relate these ideas to those well known in the literature as ‘path dependency’ and ‘lock-ins’ (cf. Arthur, 1989), drawing attention to the factors that influence technological change. Hans Harbers (2005) understands co-production as the mutual constitution of science and technology, and society, without any of the two being sufficient to explain social order or scientific and technological developments; in his edited book, co-production is analysed as an issue of distribution of agency between various human and nonhuman actors.

In *Re-Thinking Science*, Helga Nowotny and colleagues (2001) present an account of the ‘co-evolution of science and society.’ Their analysis is a conceptualization of the changing and dynamic relationship between society and science. They consider society and science as separate domains, although subject to the same driving forces, and see the demarcation between the two as becoming eroded and porous. Pestre (2003) puts into question their account of Mode 2 as a recent development and draws attention to the historical processes that have been taking place since the last five centuries, and remark on the role of social (in particular, social interests), political and economic factors in such an evolution.<sup>35</sup> In *Re-Thinking Science* the authors identify five parameters that affect science and society. First, as innovation becomes more ubiquitous, in a Schumpeterian ‘creative destruction’ (Schumpeter, 1942) fashion that extends to most facets of western society, uncertainty increases. This leads to the creation of multiple futures with different choices for citizens, but the authors notice that an unquestioned commitment to innovation tries to narrow down such uncertainties. Second, they note that the features of a ‘new economic rationality’, according to the logic of financial markets in which future profits are traded in the present have manifested in science, where the benefits and profits of basic research are anticipated and traded in the present. Third, the future is being experienced as an extended present, which can be anticipated and occupied. Moreover, the pace in which science and society advance becomes desynchronized. In this sense, an instrumental-utilitarian attitude towards science and technology yields problems of distribution of priorities and benefits of research, such as with pharmaceutical drugs for neglected diseases. The fourth parameter relates to space, including distance, and the global-local context. Knowledge production is becoming more common which in turn defies the universality of science. Moreover, the authors refer to social distance as varying awareness of the uncertainties produced by science and the composition of society, in terms of positions in society, imaginaries, and feelings of exclusion. This can reinforce the undermining of trust in institutions. Lastly, the authors refer

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<sup>35</sup> For a concise summary of the distinction between Mode 1 and Mode 2, see Nowotny, Scott, & Gibbons (2003). For a critical analysis of the Mode 1-2 synthesis, see Hessels & van Lente (2008).

to the “self-organising capacity of science and society” (ibid., p. 43), in which science and society are becoming more complex, and incorporate processes of social reflexivity.

Alan Irwin (2001) articulates the term ‘co-construction’ as a need to move beyond the dualism or dichotomy between realism and constructivism that has characterized the social sciences. Irwin invites readers to think about the environment in sociological terms as “actively generated co-constructions” (ibid., p. 173) to denote the process by which the natural and the social are co-constructed in “environmentally related practices and particular contexts.” The value of this concept lies in bringing attention to the multiple experiences of those involved in environmental controversies and how they make sense of the world. The result is better sociological analysis, opening avenues for “reflexive and democratic engagement” (ibid., p. 183). A similar critique to the duality of representation of reality argues that debates between objectivists and relativists have approached a dead-end, focusing on epistemic matters and leaving aside political questions (Demeritt, 1996). Demeritt highlights the “need to imagine some other kind of relationship to nature besides the reification of objectivity and the productionism of relativism.” (ibid., p. 497). Putting dualisms aside (i.e., natural/artificial, mind/body), he rejects the notion that either nature or society can exist as pre-existing transcendences. According to him, a richer vocabulary to think about the world is required, and in this direction Latour and Haraway with their work on Actor-Network Theory and cyborgs, respectively, have achieved important progress.

Continuing with dualisms, in the 1993 book *We Have Never Been Modern*, Bruno Latour questions the boundaries for thinking about modernity and postmodernism, and calls for an abandonment of thinking in terms of ‘dichotomies’ of nature and culture, or nature and society. For Latour, the explanations provided by SSK account only for the ‘social’ in phenomena of the world and hold that truth and falsehood cannot be explained by recurring to explanations based on ‘nature.’ Both nature and society must be explained by the same principles, both considered as being constructed, and not taken as given (the realist interpretation). Latour is keen on developing resources to understand the modern world (replacing the conceptual toolkit that has been developed since the Enlightenment). His diagnosis is centred around an official *Constitution* that distinguishes between humans and nonhumans, and between the work of ‘purification’ and ‘mediation.’

The co-productionist thinking of Latour is most evident in his assertion that nature and society cannot be used to explain phenomena but are the consequence of the stabilization of objects of external reality and subjects of society. Hence, both nature and culture must be studied as they are produced simultaneously, or “the conjoined production of one nature–culture” (ibid., p. 107), in terms of collectives, which allows us to free our thinking from dualisms (i.e., human–machine, male–female, person–fetus, and life–death); collectives are

constituted by both humans and nonhumans. Hence, nature nor culture are not to be used as explanatory factors, rather, the analyst must explain the (co-)production of nature–culture. This leads us into the realm of networks and actants, where it is important to consider the size of the collectives. However, he is not clear as to how to delimit one collective from another, or the role of the analyst in describing a network. Whether we are studying collectives or networks, the important questions are what constitutes them, what type of nonhumans are enlisted, what alliances are formed, and further repertoire provided by Actor-Network Theory (cf. Latour, 1987).

Luigi Pellizzoni (2014) also situates co-production in the constructivism/realism debate, arguing that similar approaches have been proposed in Marxist political ecology, feminist studies, critical realism, and environmental sociology. In summary “co-production scholars purport a ‘post-constructionist’ sort of realism, which rejects the idea of truth as correspondence to an immutable world but rejects the idea that language or discourse is the constitutive feature of phenomenal reality” (ibid., p. 857). From his mapping efforts, he suggests that progress in ontologies and representation should continue in the direction of “new materialism” (cf. Coole & Frost, 2010). Similar to other authors, Pellizzoni’s reason to not settle on co-productionist thinking is its potential to be co-opted for the wrong causes, such as the justification of environmental aggressions. Studies in new materialism have a remarkable similarity to propositions in STS, such as an emphasis on the agency of nonhumans, and the role of the body in political activity. Its theoretical foundation aims to spark debates based on realism, that align with recent developments in the sciences (i.e., quantum mechanics, biotechnology) that have a repercussion in social thought about global capitalism, power, and environmental affairs (Coole & Frost, 2010).

### 2.2.2 Origins of co-production

The notion that science is both a social and political activity has been one of the core tenets of STS. The term comes from a body of literature that has reflects on the intersection of knowledge production and the social and political conditions for its production. A classic study on the subject is Shapin & Schaffer's (1985) seminal work *Leviathan and the Air-Pump*, a study of a controversy over the prevailing political regime in XVII century Britain. They argue (p. 15):

Solutions to the problem of knowledge are embedded within practical solutions to the problem of social order, and that different practical solutions to the problem of social order encapsulate contrasting practical solutions to the problem of knowledge.

Their argument is based on their observations of a historical context when experimental science became a viable alternative to natural philosophy and ecclesiastic theology for

producing knowledge. For Hobbes, natural philosophy was bound to be free of authority and particular interests, unlike ecclesiastic theology. His philosophy was aligned to the goal of achieving public peace, ensuring no dissent was possible. There was no room for questioning or freedom, and this was possible because natural philosophy was understood as a cause and effect endeavour, where the problem was to establish solid and agreed upon foundations. This makes it easy to understand why Hobbes ardently opposed Boyle's new paradigm of experimentation.

Boyle saw experimentation as the mechanism for producing matters of fact which included not only the use of instrumentation (such as the Air-Pump), but new social conventions that highlighted the importance of witnessing, and replication. There would be a space for deliberation over the working of experiments, mostly public (although restricted to members of The Royal Society). By doing so, experimentalists aimed to show a model of how a community could have open discourse to achieve consensus, without the need for authority, therefore avoiding conflict and reaching peace, so needed in Restoration England. Hence, the newly established laboratory would become an example for how society could be ordered. Its proper functioning, though, also depended on having the space and lack of oversight for experimentalists to pursue their own interests and providing solutions of value for society, such as improved artillery or brewery methods. The main lesson is that the polity, or securing of social order, was compatible with the generation of knowledge by experimentation; they are solutions to a common problem, not necessarily reinforcing each other. It is also noteworthy how Boyle and Hobbes disagreed about knowledge in public. For Hobbes, philosophical enquiry had no space and could be practiced anywhere, as long as there was the authority to do so. For Boyle, public performances of experiments, or witnessing, was a requirement for the validity and dissemination of knowledge, but this was supposed to take place in spaces dedicated to this end, which would eventually transform into the laboratory. Not anyone had the chance to attend such gatherings in which experiments were conducted.

I have summarized Shapin and Schaffer's book at length because their thesis of social and political order being co-produced has influenced co-productionist thinking that has inspired in STS a more political inclination attentive to power. For instance, Sheila Jasanoff (1996) engages in debates over the neutrality of the analyst in the sociology of scientific knowledge (Scott et al., 1990). For her, SSK has been too focused on a framework of controversy, which ignores the social and political disputes that are consequence of such controversies. She makes the point that relativist SSK ways of analysis are misused in US courts by entities that have excessive power, like US corporations, which reflect the use of science in American political life. Moving beyond a framework of controversy is justified as:



The project of politics is at once deeper and broader. It is to understand how entire edifices of natural knowledge and social order build upon each other as human societies endure, evolve, change, and sometimes crumble over time ... a symmetrical methodological approach requires us to use the same resources in explicating closure, stability and change in people's *knowledge of the world* and their organization of *life in the world*, for each is constitutive of the other." (Jasanoff, 1996: 396-397; emphasis original)

In the same issue of *Social Studies of Science*, Harry Collins (1996) responds to Scott, Richards and Martin (1990). He argues that SSK's commitment to symmetry is desirable as an aspiration, in order to achieve social scientific rigor. He also finds difficulties with determining what side is the weaker side in a controversy, from his own experience studying gravitation waves. Collins sees SSK's symmetry as a methodological consideration, whereas Jasanoff is interested in moving beyond a framework of controversy, of studying controversies in science *and* the public.

The proposition of the 'idiom' of co-production of Sheila Jasanoff goes beyond debates of realism versus constructivism. Rather than a theory, co-production in her terms is "an idiom — a way of interpreting and accounting for complex phenomena so as to avoid the strategic deletions and omissions of most other approaches in the social sciences." (Jasanoff, 2004b: 3). She defines co-production as "the ways in which we know and represent the world (both nature and society) are inseparable from the ways in which we choose to live in it" (Jasanoff, 2004b: 2). In the second chapter of *States of Knowledge*, Jasanoff (2004a) makes the theoretical case for co-production, classifying major works in STS that represent components of this framework, and establishing connections with wider literature, mainly political science. Co-production not only seeks to dismantle any *a priori* place for the social or the natural in accounts of scientific knowledge in society. It seeks to establish a dialogue between STS and other disciplines. Some of the questions asked have to do with making visible the "emergence of new authority structures and forms of governance, the selective durability and self-replication of cultures, and the bases of expert conflict over knowledge in rational, democratic societies" (ibid., p. 42). Jasanoff distinguishes between two 'streams' of co-production, one *constitutive*, the other *interactional*. The former is related to metaphysics, representation and questions of meaning. Briefly defined as

Primarily concerned with the ways in which stability is created and maintained, particularly for emergent phenomena, whether in a site where knowledge is made, such as a research laboratory, hospital or legal proceeding, or around a novel technoscientific object, such as the human genome or a periodic table for chemicals. At the most basic level, the constitutive strain in S&TS seeks to account for how people perceive elements of nature and society, and how they go about relegating part of their experience and observation to a reality that is immutable, set apart from politics and culture (p. 18-19).

In her account, Jasanoff contrasts studies in Actor-Network Theory by Bruno Latour and Andrew Pickering, mainly because it departs from distinctions between natural and social and distinguishes between the agency of humans and non-humans. Here the issue is what links and holds networks together, what makes them durable, and provides concepts useful

to think of power, such as ‘centres of calculation.’ Jasanoff claims that Actor-Network Theory could pay more attention to the context in which the networks are formed, in particular to the role of culture, power, beliefs, or ideologies. Jasanoff’s co-production facilitates links with other studies in political theory, for example by Benedict Anderson and James Scott, who question how representations (like nationhood, or the legibility of citizens and economic production) are managed and operated in the interface between the state and its citizens. A second strand more concerned with epistemology, termed *interactional*, addresses questions of how technology is put to the service of the state, and the role it plays in establishing political order.

In her essay, Jasanoff also describes four pathways through which co-production occurs: making identities, institutions, discourses and representations. I concentrate on ‘*making discourses*’ (Jasanoff 2004a: 40) because it is the most relevant for this dissertation. The emergent field of xenobiology makes implicit not only scientific discoveries or achievements, but the development of new language that aims to persuade scientific peers and gain legitimacy from the public to advance the agenda of the field. As Jasanoff points out, “In the process [of appropriating existing discourses and their retailoring to suit new needs], scientific language often takes on board the tacit models of nature, society, culture or humanity that are current at any time within a given social order” (ibid., p. 41).

The rationale behind co-production can be seen as reinvigorating questions that have been forgotten in STS, to gain richer explanations and descriptions of the interface between human agency, ordering devices (such as artefacts, experts or laws), and the reconfiguration of nature and society. Questions about power and culture in constituting order go hand in hand with a conceptual repertoire that includes the role of material objects, the diversity of scientific and technological practices, and the stability or contestation of networks; as well as memories, identities, representations, imaginations, beliefs, values, and ideologies. However, Jasanoff rejects black-boxing, not only of technologies, but of concepts drawn from political science, such as modernity, the state, or capital.

Central to co-productionist thinking is a greater understanding of power, how it affects the constitutions of networks, how it is influenced by knowledge, what constraints it or enables it, and whom it empowers, to name a few considerations. However, she does not specify the meaning of power or how to look for it. This is expected as the co-production framework aims to highlight not the study of power itself, but how elements that constitute science and technology, such as expertise, objects, artefacts, regulation, institutions, and imaginaries, play a role in shaping it. This passage about questions in co-production is telling: “how power originates, where it gets lodged, who wields it, by what means, and with what effect within the complex networks of contemporary societies” (Jasanoff, 2004b: 5).

Efforts to build upon co-production into a ‘theory’ include its connection with Mary Douglas’ cultural theory (Swedlow, 2012), specifying and predicting “political cultural conditions under which the coproduction of science, social order, and scientific, cultural, and policy change, are likely to occur” (p. 172). By studying the conservation of spotted owls and management of old-growth forest ecosystems in the Pacific northwest, the author points out a transformation from hierarchical structures to egalitarian ones, both at the level of individual identities and institutions, in line with cultural theory; these changes were brought along with representation of nature, mainly from aiming for sustainability in production of forest commodities to management at the ecosystem level.

Co-production is broad in its parameters and coverage; hence it has been interpreted (or misinterpreted) in different ways. Studies of co-production in laboratories are scarce and especially relevant, since one core question in the framework of co-production is ‘where to look for co-production’, for example the laboratory, organizations, or nations, or even more heterogeneous assemblages (Jasanoff, 2004b: 5). Few studies have studied laboratories as a site of co-production, including Doubleday (2007), who provides an account of a nanoscience laboratory in which through forms of accountability that are negotiated, either with funding, or with wider society (through collaboration with social scientists), a vision of science and innovation is reinforced, in which basic science and industrial applications go hand to hand, and the public act as passive recipients of technological products. He denotes the laboratory as a space “in which both social and technical worlds are co-produced” (p. 167), and where concepts of citizenship are elaborated, and the potential for controversy is assessed and resolved.

In summary, co-production serves as a sensitizing concept that departs the social study of science and technology from technological determinism to emphasize a more systemic understanding of how technology and society ‘co-produce’ each other, providing a more nuanced political analysis than the social constructivist angle of STS. Co-production in this thesis is reflected in the approach to science and the public, and the influence of political and cultural contexts in shaping the trajectories of innovation. Epistemic and normative understandings of the world are co-produced. The ideas and objects produced by xenobiologists carry meanings and values about society of which I provide an account.

## **2.3 Future-oriented imaginaries and imagination**

### **2.3.1 Imaginaries in the social sciences**

Imagination is an essential component in the production of knowledge and technology, and an overarching theme in this thesis. Creating imaginaries and visions are part of the

practices that scientists engage in laboratories and in their fields of expertise. The concept of *imaginary* is useful to understand how scientists think about science and society and the power with which they shape the world. First, I provide an overview of how the concept has been articulated by major thinkers in the social sciences, before turning to imaginaries that deal with technoscience. I stand on the concept(s) of imaginaries because they combine the collective aspect of scientific enterprise, as well as the practices, behaviours, and agency of actors involved in knowledge production. The orientation toward the future of the imaginaries I emphasize is useful because xenobiology builds on many assumptions and visions that may reify in the near future. Currently, they are expressed as narratives, discourses and rhetorical devices that are performative as they guide experimentation in the field.

The Greek-French philosopher Cornelius Castoriadis analysed the ‘social imaginary’ in his seminal book *The Imaginary Institution of Society* (1997b [1975]). He was concerned with the reasons behind differences among societies, and social change. He was concerned with the role of the imaginary in the (material nature) of social life, especially on how it defines institutions and their functions. Imaginaries are wide-ranging and at the core of society; they are ‘autonomous’ and have been with societies from their beginnings. They are also akin to a ‘world view’ (Castoriadis 1997: 160-161). Dilip Gaönkar (2002) stresses that Castoriadis’ imaginary is related to symbols that people imagine and serve as world-making collective agents. For our purposes, bringing the imaginary from the abstraction to a more workable form is indispensable, and so arises the question of where imaginaries reside, or who actually *imagines* them; Strauss (2006: 326) sheds light on this issue:

Societies are not creatures who imagine, but people do. What Castoriadis called ‘social imaginaries’, then, may be the conceptions of many members of a social group –or, sometimes, dominant members of a social group, or ideologists of a social group– repeated in multiple or influential social contexts, learned from participation in shared social practices and exposure to shared discourses and symbols.

A different group of authors have given different meanings to the (social) imaginary. In the book *Imagined Communities*, Benedict Anderson (2006 [1983]) argues that imaginaries account for the rise of Nationalism (an anomaly) and the larger question of what keeps communities together. ‘Print capitalism,’ the combination of a market for printed texts and the mass production of texts (books and newspapers) became a mechanism for people in a society to keep a conversation about the same ideas and identity, creating a space for a ‘common discourse;’ this was only possible by the invention of Gutenberg’s press, which made available books and other written forms to a wide proportion of the population in ways that were not possible before. For him, the nation serves as a collective fiction that unifies aspirations and goals of different peoples over a common purpose, like the formation and endurance of a state, aided by technologies such as the circulation of printed words like

newspapers and novels. Nevertheless, Anderson seems to take for granted concepts like the nation, rather than explaining how different imaginaries and practices constitute the nation.

On a different line of thought, Charles Taylor and Arjun Appadurai's ideas on imaginaries converge. Appadurai's (1996) *Modernity Enlarged* is concerned with globalization and the (imminent) end of the nation-state, and features of new modernity. Two forces are driving this process, mass migration and (electronic) mass media, where imagination plays a new role in social life. For Appadurai,

The image, the imagined, the imaginary—these are all terms that direct us to something critical and new in global cultural processes: *the imagination as a social practice*. No longer mere fantasy (opium for the masses whose real work is elsewhere), no longer simple escape (from a world defined principally by more concrete purposes and structures), no longer elite pastime (thus not relevant to the lives of ordinary people), and no longer mere contemplation (irrelevant for new forms of desire and subjectivity), the imagination has become an organized field of social practices, a form of work (in the sense of both labor and culturally organized practice), and a form of negotiation between sites of agency (individuals) globally defined fields of possibility (Appadurai, 1996: 31).

Broad historical periods have been the subjects of study by the authors mentioned above. Charles Taylor is not an exception, as he analyses the transition to modernity, but both in terms of Western modernity itself, and of multiple 'modernities.' This is the starting point of start for elaborating further on the 'imaginary', expanding it upon what Heidegger and Wittgenstein call 'the background.' Taylor aims to trace the passage to modernity, as the transformation (or 'infiltration') of a set of connected ideas (theory) into a 'social imaginary' (Taylor, 2002). He attributes the instauration of a new moral order based on the mutual benefit of equal participants (and with it, the rise of individuality as opposed to hierarchy/community), which is accompanied by the creation of an economy and a 'public sphere.' Imaginaries are centred on the public, the tissue of society. His words are the following:

[By social imaginary] I am thinking, rather, of the ways people imagine their social existence, how they fit together with others, how things go on between them and their fellows, the expectations and are normally met, and the deeper normative notions and images that underlie these expectations", to which he adds that the term imaginary is "carried in images, stories and legends (Taylor, 2004: 23).

Taylor provides two examples of social imaginaries in action, related to how people vote, and how people organize for demonstration (protest) (Taylor, 2004: 24-26). In both instances, people know how to organize, what they are supposed to do, and what their actions imply (i.e., knowing that a demonstration is an act of free speech).

I end this section with the discussion on George Marcus' (1995) edited volume titled *Technoscientific Imaginaries*. The main theme of the book is the changing conditions for science and technology at the *fin-de-siècle*. As Marcus puts it, 'technoscientific imaginaries' bear relation with "immediate associations of scientific practice with the 'visual', or 'imaging', on one hand, and with visionary, innovative, imagination, on the other—an orientation to

imagining futures and the fantastic.” (ibid., p. 3). This seems to keep distance from the work on (social) imaginaries discussed above but has much to do with the component of ‘visions of desirable futures’ engrained in ‘sociotechnical imaginaries.’

Before continuing, a note on metaphors is helpful, because they help understand the visions, narratives and metaphors that xenobiologists put forward, like “navigating unknown biological worlds” (**Chapter four**). They are part of a cultural toolkit for constructing novel meanings about biotechnology in xenobiology. They are important for how we conceptualize problems (Thibodeau & Boroditsky, 2011) and play a role as cognitive and linguistic tools that allow humans the creation of new meanings, based on pre-existing associations; they facilitate thinking about the world and acting on the world (Lakoff & Johnson, 1980). Synthetic biology is a field that has advanced while making use of various metaphors. In their study of how metaphors of synthetic biology are portrayed in the media, Hellsten & Nerlich (2011) found that metaphors use familiar language of information theory (i.e., codes, software, book of life), as well as historical points of reference such as the industrial revolution, which provides a context for standardization, assembly and control. They note that such metaphors may cause discomfort in the public sphere and suggest a metaphorical framing of synthetic biology that is less controlling of processes of life.

Having provided an overview of the literature on imaginaries in political science and anthropology, and its various interpretations, it is time to move to the concept of sociotechnical imaginaries, which emphasizes the collective aspect and future-orientation of world-making through science and technology.

### 2.3.2 Sociotechnical imaginaries

Sheila Jasanoff and Sang-Hyun Kim formulated the concept of *sociotechnical imaginaries* in order to bring attention to the relation between science and technology, and politics and culture. The concept is closely related to the idiom of “co-production” (Jasanoff, 2004b) and aims to make an important shift from a focus on regulation to innovation policies (Jasanoff et al., 2006). Jasanoff & Kim (2009: 120) defined sociotechnical imaginaries as “collectively imagined forms of social life and social order reflected in the design and fulfilment of nation-specific scientific and/or technological projects.” And added, “Imaginaries, in this sense, at once describe attainable futures and prescribe futures that states believe ought to be attained”, and guide the production of knowledge. Sociotechnical imaginaries drive technological trajectories, represent visions of how technology should be developed for good or bad and very importantly, guide how states support visions of ‘where-to-get-to’ visions. A more recent definition of sociotechnical imaginaries places more emphasis on temporality, in terms of

how science and technology influence the social order through time, perceived and influenced by multiple generations, has a long-term impact on the long term. In the words of Jasanoff (2015a: 4), sociotechnical imaginaries consist of the following:

Collectively held, institutionally stabilized, and publicly performed *visions of desirable futures*, animated by shared understandings of forms of social life and social order attainable through, and supportive of, advances in science in technology (emphasis added).

The original delineation of sociotechnical imaginaries studied how technology contributes to nation-building in the case of national policies and political culture of the United States and South Korea (Jasanoff & Kim, 2009). It is tempting to think of sociotechnical imaginaries as the reason for the implementation of science and technology policies, and the ends or socio-political outcomes that these were expected to achieve. But as they are proposed, they escape such rigidity and can be found as the combination of speeches, policies, laws, actions, and other elements to be found in the political world. The concept is highly flexible, and does not predispose categories or prefabricated concepts in the form a framework would signal. It is neither it is restricted to national innovation policies, nor the history of corporations, rather, it is an analytical tool to understand distributions of power and agency.

According to their original conception, certain characteristics delineate sociotechnical imaginaries. First, they are a 'cultural resource' that has an immediate impact on the future. They do so by dictating what is desirable and which direction to take within the commonly held hope that technology leads to social progress. In this regard, sociotechnical imaginaries "encode not only visions of what is attainable through science and technology, but also of how life ought, or ought not, to be lived" (Jasanoff, 2015a: 4). This desirability comes loaded with normative aims, as technology is most usually performed with beneficial ends in mind (although these may not necessarily be distributed for the benefit of all). Second, they are collectively held, and as such, although they could be attributed to the visions of specific actors or institutions, they must reach a wider audience that must adopt them, and in the process they need to be 're-enacted' if they are to be preserved over time (Felt, 2015). Third, at a given point in time, competing sociotechnical imaginaries may be present, and they even could repel each other; in explaining why some prevail over others, or why they may differ among themselves, lies the analytic potential of the concept; the literature has been mostly preoccupied with sociotechnical imaginaries in terms of how they are originated, pursued, preserved in time, made more durable, and also, how they compete with each other (i.e., Levidow & Papaioannou, 2013a). Fourth, sociotechnical imaginaries are performative, they have the capacity to lead and orient actions and interventions. The future is represented in the present and is imagined. As such, they can lead to collective action. Last, sociotechnical imaginaries do not necessarily originate from the top-down, that is, from institutions to

citizens. On the contrary, they can originate in the public, resembling national culture, and in the process, become embedded in national culture (cf. Felt, 2015).

Reflecting on the dynamics of sociotechnical imaginaries, Stephen Hilgartner (2015) suggests that previous to the collective holding of a sociotechnical imaginary, it is possible to identify ‘sociotechnical vanguards,’ understood as visions of the future held by a small group, which seek to permeate a larger collective. If they reach a larger collective, they can become a sociotechnical imaginary. Hilgartner defines the concept of ‘sociotechnical vanguard’ as:

Relatively small collectives that formulate and act intentionally to realize particular sociotechnical visions of the future that have yet to be accepted by wider collectives, such as the nation. These vanguards and their individual leaders typically assume a visionary role, performing the identity of one who possesses superior knowledge of emerging technologies and aspires to realize their desirable potential. ... one finds multiple vanguards that overlap incompletely, promoting sociotechnical visions that are often only partially shared. (ibid., p. 37)

Hilgartner supports his concept by analysing the BioBricks initiative in synthetic biology. He suggests that vanguards draw on existing sociotechnical imaginaries, and BioBricks rely upon a national imaginary of ‘America the innovator.’ It is important to note that visions alone are sufficient to reify and achieve a shared imaginary; BioBricks required a series of activities to institutionalize themselves, such as defining technical standards, legal frameworks, and developing educational material. As other authors have also suggested, Hilgartner notes the contested nature of vanguards. Imagination in synthetic biology draws on existing templates, which also bring along practices, ways of doing things (like decoupling and modularity), and forms of circulation, like start-up culture, and individual rights. On the contrary, proponents of BioBricks also have tapped into a discourse of openness related to biohacking culture, and of playing with the possibilities of life.

Likewise, Joan Fujimura (2011) explores on a more specific level the conceptual and epistemic tools associated with systems biology. For this task she explores the ‘technobiological imaginaries’ that systems biologists use as they grapple with complexities in biology, explaining how they conceptualize cells and cells’ interactions with their environment as part of molecular networks, as if they were engineering systems. She addresses how cybernetic and systems theories have been used to develop systems biology, as a set of technobiological imaginaries used to produce renderings of nature. This engenders a representation of nature with ideas of dominance and hierarchy. For her, understanding what happens at the border crossing between engineered and biological systems, what is lost (excised, distorted, transformed, deleted, or added) in the process is crucial for understanding technobiological imaginaries and their potential consequences. In a similar vein, Fujimura’s (2003) ‘future imaginary’ refers to a rhetorical strategy that scientists employ to advocate a transformative vision of their society. Future imaginaries are similar to sociotechnical imaginaries with their attention to desirables futures, but Fujimura does not place emphasis



on collective aspects of the imaginary. In her study, Fujimura analyses the rhetoric employed by two prestigious Japanese scientists (and entrepreneurs). Among them is a famous molecular biologist who conceives genomics as the means for a transformation of Western values, and the return of Japanese culture to its 'Shinto.' Similar is the case of Kitano Hiroaki, an influential figure in robotics and 'systems biology,' for whom his vision of systems biology is compatible with Japanese culture, partly to attract support from funding agencies and recruit highly capable personnel. Other studies have focused on how visions of the future, in terms of social, economic and environmental means, shape the development of technologies, including 'Small Nuclear Reactors' (SMR) (Sovacool & Ramana, 2015) and a 'hydrogen economy' of energy production (Eames et al., 2006).

Relevant for the study of sociotechnical imaginaries in xenobiology, Ben Hurlbut (2015) elaborates on how sociotechnical imaginaries not only relate to the future, but also to the past, reinterpreting, and re-enacting it (more in **Chapter five**). The contrast with the studies mentioned above is striking. Hurlbut focuses on governance, looking at the "ways sociotechnical imaginaries can shape the organization of practices of governance" (ibid., p. 142). His analysis focuses on two sides. In the first, he explains why 'Asilomar-in-memory'<sup>36</sup> as an imaginary of 'governable emergence' became crystallized in memory, and is continuously invoked for new emerging technologies. In the second, he delves into what such imaginary reflects about current ideas and practices of democracy, as well as governance of technology (and risk). He concludes that a narrative has crystallized in 'memory' of how the governance of the relation between science and society should take place. It consists of technology as inherently normative, with scientists being better equipped than anyone else to foresee the impacts of a technology (usually positive), and any debate should be brought down to quantification of risk (at least in the United States). Accordingly, what is to be contained is not so much a biological 'risk' per se, but the risk presented by the public and the law to inhibit the development of a nascent field. In other words, it is science which must be protected from society. This echoes in Jasanoff and Kim's (2013) study that suggests that imaginaries of risk have not been subject to sufficient public scrutiny in countries like the United States and Korea; at its very root, this imaginary is about the shading of deliberation in democracy.

The imaginary of 'Asilomar-in-Memory' is also justified because it captures a mode of governance favoured by the scientific and policymaking communities because it is aligned with the notion that the "government cannot shape but can only react to technoscientific

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<sup>36</sup> In the Asilomar conference of 1975, pioneers in the emerging field of genetic engineering gathered to decide on recommendations for how to contain the hazard presented by genetically modified organisms (see Berg et al., 1975).

change” (Hurlbut 2015: 137). It involves anxiety toward letting a promising technology dissipate, and the need to nurture it as the role of the government; more than to protect its citizens. As Hurlbut argues, such an imaginary fits with American ‘civic epistemology’, and “resonates with the constitutional commitment in American political culture to the separation of science and the state” (citing Jasanoff, 2005). This coincides with assertion of an American sociotechnical imaginary in which a ‘technology’s benefits are seen as unbounded while risks are framed as limited and manageable’ (Jasanoff & Kim, 2013: 190).

### 2.3.3 Methodological aspects of sociotechnical imaginaries

It is important to address methodological considerations for the study of sociotechnical imaginaries, given they are central in the theoretical toolkit of this dissertation. However, when referring to (sociotechnical) imaginaries, it is not simple to define the object of study. What can be identified as an imaginary? How can the concept be operationalized? Imaginaries do not need to be measurable or observable, but rather help understanding other objects, narratives and modes of action. They are different from *discourse*, which Hajer (2006: 67) defines as “an ensemble of ideas, concepts, and categories through which meaning is given to social and physical phenomena, and which is produced and reproduced through and identifiable set of practices.” Discourses are useful to align actors towards a shared interest or goal. Technoscience, given its close relation to materiality, objects and experimentation, requires a different lens. Sociotechnical imaginaries provide a conceptual framework that situates technologies within material, moral and social landscapes. The result of technology’s manipulation of nature and technology depends on modes of organization and normative dimensions (Jasanoff, 2015a). Such emphasis on the reconfigurations of power brought by technology distances the concept from similar approximations to imaginaries of technoscience, such as technoscientific imaginaries (Marcus, 1995). Marcus situates imaginaries in the materiality of scientific practice,

Interested in the imaginaries of scientists more closely to their current positionings, practices, and ambiguous locations in which the varied kinds of science they do are possible at all. This is a socially and culturally embedded sense of the imaginary that indeed looks to the future possibility through technoscientific innovation but is equally constrained by the very present conditions of scientific work (ibid., p. 4).

The attention to materiality in regard to sociotechnical imaginaries is one element that this dissertation explores in depth. The laboratory has been seldom studied as a site for the analysis of sociotechnical imaginaries, as other approaches have been preferred. Sheila Jasanoff favours a historical approach to sociotechnical imaginaries, to examine their stability and maintenance, as well as their study in policy discourses, texts, and other modes of expression at the collective level. For instance, Jasanoff & Kim (2009: 123) write,

Imaginarities, in our view, are not the same as policy agendas. They are less explicit, less issue-specific, less goal-directed, less politically accountable, and less instrumental; *they reside in the reservoir of norms and discourses, metaphors and cultural meanings out of which actors build their policy preferences*. Neither are imaginaries simply master narratives that justify scientific or technological investment, such as the pervasive modern narrative that equates science with progress. Unlike master narratives, which are often extrapolated from past events and serve explanatory or justificatory purposes, imaginaries are instrumental and futuristic: they project visions of what is good, desirable, and worth attaining for a political community; they articulate feasible futures (emphasis added).

Nevertheless, scientists can be promoters and magnifiers of sociotechnical imaginaries. The laboratory also serves as a place where imaginaries are isolated and maintained, perpetuated through material practices that are tangled with ideas, practices, commitments, and values. Gjefsen & Fisher (2014: 422-423) conceive the laboratory as a source of cultural production, ‘socializing countless experts-in-the-making in practices and conditioning expectations in ways that potentially implicate broader socio-technical imaginaries.’

The laboratory has been a fruitful site for observation by STS analysts, whom originally focused ethnographies on the production of facts and the interpretation of evidence and consistency were dependent on contingent events, negotiation and local decision-making processes (cf. Doing, 2008). The relation between the laboratory and the ‘outside’ world has been a theoretical and methodological question that has permeated laboratory ethnographies. Bruno Latour and Steve Woolgar (1986) asserted in the postscript to the paper-back printing of *Laboratory Life* that they initially restricted themselves to studying the delimited space of the laboratory, as a step required to demystify the production of facts and knowledge in the laboratory. The authors saw this as a temporary step in STS, toward conceptualizing the laboratory as a point of passage for a diverse array of actors. For David Hess (2001), what he calls ‘second generation’ STS ethnographies have turned to social problems, extending the physical space of scientists to study lay groups, social movements, and political activities. Moreover, he argues that in this second generation the construction problem turns to

How social and technical factors are interwoven in knowledge and technology production (social construction) or how sociotechnical networks and societies are mutually constituted (co-construction) to how cultural meanings or legitimating power relations are embedded in science and technology (cultural and political construction) and how different actors interpret science and technology (reconstruction) (ibid., p. 240).

For Hilgartner (2015), only when a vanguard vision (held by a relatively small number of individuals—visionaries) is widely adopted it becomes a sociotechnical imaginary; this makes the question of how sociotechnical imaginaries circulate or travel, particularly important. In the same vein “ideas about scientific and technological futures need to gain assent outside such bounded communities in order to become full-fledged imaginaries” (Jasanoff, 2015b: 326). The circulation of ideas and discourses about certain sociotechnical

imaginaries in a laboratory can potentially signal their collective character. This dissertation aims to complement this insight. From a vantage point, the laboratory is a site where sociotechnical imaginaries travel and circulate, and stay, through their association with material practices and ways of approaching experiments and assumptions about biology. The laboratory then serves both as a space for cultural production and the exchange of ideas about facts and problem solving, and a *recipient* of ideas already in circulation elsewhere about the role of science and technology in society; moreover, a space where ordering takes place (Law, 1993).

The analyst faces a challenge of keeping track of events in the laboratory while tracing associations and connections with the cultural and political context in which the events take place. This is further complicated by scientists' disposition to focus on the inner workings of the laboratory, rather than be aware about the wider implications of their work. Recently, the importance of studying and understanding sociotechnical imaginaries for exercises sociotechnical integration has been shown for developing socially reflexive capacities in participants and enable novel cultural and material pathways (Richter et al., 2017). Rather than a site for studying the temporal and spatial dynamics of sociotechnical imaginaries, the laboratory can prove fruitful as a site to study their circulation and extension (Jasanoff, 2015b). In short, in what terms do sociotechnical imaginaries enter the laboratory and circulate? How individual visions can percolate to collective held objectives? Laboratory ethnographies in STS suggest that a closer understanding of the relationship between relationship between metaphors (of which there are plenty in xenobiology) and materiality can be gained, an underexamined aspect of sociotechnical imaginaries.

#### **2.3.4 Imagining the public**

Imagination in science, as I argue in this thesis, not only includes visions of what constitutes a desirable sociotechnical order, but how publics can react and get used to novel developments in science and technology. Hence, it is necessary to account for how the 'public' is constructed, as this bears a major role in the trajectories of science. Wynne (2005) proposes 'public science' to acknowledge that science and knowledge production are constructed based on the public's perception, a projection of public concerns by scientists. Wynne defines 'public science' as "scientific knowledge in which we may identify such implicit human–public dimensions as part of the science itself" (ibid., p. 68-69); as well as "scientific knowledge conceived and constructed with an implicit imagination of arenas of public deployment, and of public audiences" (ibid., p. 81), which requires distinction from a traditional conception of scientific knowledge as laboratory knowledge that is only later applied." A case that builds upon co-production and public science is the 'co-production of

uncertainty' (Stilgoe, 2007), concerning the mobile phone controversy in the UK. Recommendations over the use of mobile phones and mobile phone masts was influenced by how scientific advisors in the UK interpreted public concerns. Interestingly, scientific advice took a precautionary stance, not justified by science—as in the use of mobile phones by children—in order to comply with their construction of the 'publics.' Another case relates to the 'Barcoding of Life Initiative,' in which 'public science' takes place but with an imagined public (Ellis, Waterton, & Wynne, 2010). Nevertheless, a clear picture of how science and society, or the public, feed each other, also requires also an understanding of imaginaries of decision-makers (Nowotny, 2014).

Irwin (2006) argues that public talk is flexible and must be constructed to be open to interpretation. According to him, "There [is] no direct or context-free access to 'the public'", and "public opinion is both elusive and open to multiple constructions, including claims and counter-claims about what the public 'really' thinks and what the 'real public' might be" (ibid., p. 314). Indeed, the identified 'deficit model' in policy circles involves a form of imagining the attitudes and knowledge of the public toward science, misinterpreting that if the public knew more about science, it would trust more technoscientific implementations (Wynne, 2006).

An important case about the construction of the public is provided by the 2003 '*GM Nation?*' debate over growing and trading commercial genetically modified crops in the UK. The debate was a result of the British government's response to what has been dubbed the 'GM controversy,' to refer to general scepticism and rejection of the cultivation and commercialization of genetically modified crops in Europe.<sup>37</sup> For Lezaun & Soneryd (2007) the construction of the ideal public in *GM Nation?* was that of an unengaged citizen, unfamiliar with genetic engineering and without prejudices. In other words, it would be a mouldable participant, as opposed to the actively engaged, likely anti-GM participant. Reynolds (2013) also analysed how 'different versions of the public were imagined and constituted.' In what he sees as a socio-material entanglement, in which both seeds and humans are enmeshed, separate British advisory bodies kept separate strands of the 'social' and the 'natural', maintaining the bifurcation of the two that Latour persistently has criticized. Moreover, Grove-White (2006) reminds us of a recurrent theme in the literature, the critique of how risk is often framed in terms of risk, to account for the GM controversy,

Relevant concerns about particular GM constructs should only be understood in terms of specific definable 'risks', that the only relevant knowledge gaps or uncertainties are those *already specifiable* in agreed scientific terms, and that when no such specifiable 'risks' (or 'uncertainties') can be identified through available scientific knowledge, there are no reasonable

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<sup>37</sup> For STS studies of the 'GM controversy', see Marris et al. 2001; Levidow 2001; Jasanoff 2005.

grounds for preventing particular new GM artefacts from being released more widely (ibid., p. 173) (Emphasis original).

Likewise, Bronson (2015) discussed how the implementation of hybrid seed innovation and genetic engineering technologies in Canada during the twentieth century was intended to alter power structures, favouring a 'neoliberal' agenda in the interest of a handful of agribusiness companies, which promoted a 'productivist' (i.e. industrial) form of farming, with negative consequences for local farming communities. It has been suggested that the framings of a debate on a specific technology (i.e., risk)— can be carried on from one technology to an incoming emerging technology (Felt, 2015), and the debate on synthetic biology can be moulded by other technologies such as nanotechnology, information technologies or genetic engineering (Torgersen & Schmidt, 2013). Claire Marris' (2014) analysed how synthetic biology stakeholders imagine the public, noting how the debate on synthetic biology is reminiscent of the GM crop controversy, without much having changed since. Marris indicates how a distinction between a 'disembodied public' —passive, malleable, immobilized, not interested in synthetic biology, and activists and members of NGOs (mobilized) pose a threat to this field. This echoes with a "*state-scientific imaginary of publics* as threatening the social (economic) order" (Welsh & Wynne, 2013: 554). In this way, public acceptability becomes an obstacle for the deployment of the promise of synthetic biology (Marris, 2014), and alternatives to overpass it are sought in scientific achievements.

Particularly important for the analysis of xenobiology is the importance of public views of nature, regardless of how they are imagined by scientists; public reception of biotechnology is a major aspect that will shape the development of xenobiology in the coming years. A group of researchers lead by Martin Bauer and George Gaskell provided insights about the reception of modern biotechnology in Europe and North America in the late 1990s (Bauer & Gaskell, 2002; Gaskell & Bauer, 2001). Their inquiry was guided by the question of why the public resist new biotechnologies, emphasising the years 1996-1999, which comprise the 'watershed' years of the great European debate on biotechnology. An important turning point was the annual cargo of soya from the U.S. to Europe, which for the first time included genetically modified soya (resistant to the herbicide glyphosate), produced by Monsanto. This stirred the public sphere of biotechnology in Europe, with consequences that have framed debates ever since. Another important event was the cloning of 'Dolly the sheep' in Edinburgh, raising questions about the limits of human manipulation of nature, and potentially humans themselves. Public opinion on biotechnology lies on a variety of factors, including risk, trust in scientific institutions and corporations, welfare of farmers, cultural attachments to food, fears about industrialization, among others. Of these factors, moral objections and interference with nature are relevant for the argument of this chapter. They constitute the kind of limits or barriers that xenobiology arguably defies.

In their study about the nature of public resistance to modern biotechnology, Nielsen, Jelsøe, & Öhman (2002) apply a segmentation between two types of arguments for public opposition to genetically modified organisms and biotechnology –‘blue’ and ‘green’–, to study the public dynamics of Europe. The ‘blue’ segment is likely to raise moral and ethical issues about biotechnology, whereas dangers and risks concern the green side. Important for our purposes, the authors propose that political discourse has focused the question of biotechnology on ‘green’ arguments, matters of risk and scientific, rather ignoring blue arguments. Nevertheless, in the United States much of human embryonic stem cell research has been restricted due to moral convictions (Hurlbut, 2017a). In xenobiology, debates in the field (framed by scientists) tend to be oriented toward managing risks, but arguably not dealing with moral aspects. Public attitudes toward biotechnology, at least in Europe, assume a critical standpoint that runs across a spectrum from rejection, to ambivalence, to optimism.

Wagner and colleagues (2002) note in their study of images and social representations of biotechnology that the notion of *Nature* underlies many of the ‘images’ (social representations of biotechnology, symbolic ways of coping with unfamiliar objects, appearing as pictures, text or forms of discourse) they identify in their study. Among the themes that they highlight can be found that nature is associated with slow and continuous development, a pace which biotechnology abruptly disrupts. Another theme is that nature can backfire, or take revenge; this does not ascribe agency to natural disasters, but conveys the notion that altering the carefully maintained balance of nature can bring unanticipated and serious consequences. Some moral arguments that question biotechnology build upon the notion that new technologies in the field allow humans to interfere with the ‘natural’ harmony of nature. Genetic engineering is considered as inappropriately ‘tinkering’ with life, altering a meaningful order of nature in which every species has its place and its purpose and where natural boundaries should not be transgressed by unnatural means’ (Wagner et al., 2002: 254).

The authors suggest that other themes of public’s association of nature with biotechnology include the question of conferring scientists the ability to manipulate the genetic makeup of humans, that is, humans interfering with human nature. This means altering the essence of what it is to be human. From a moral point of view, such manipulation also confers humans God-like powers, which may lead to ‘playing God’ and interfere in God’s plan, God’s Creation, seen as a threshold that should not be crossed. The authors also report that respondents in their study commented that the modification of nature raises a paradox, in the sense that what is special about natural life is that it cannot be ‘made.’ Nature is associated with sacred values that are threatened by biotechnological interventions,

overreaching human powers and purpose in the world. On the other hand, Wagner et al. (2001: 86-87) distinguish arguments about nature in two categories, or forms of arguments. The first, a *spiritual* form, describes how there are clear limits in nature not to be trespassed, and there is a reason (beyond our understanding) for why nature is the way it is –it has a higher purpose that must be respected. On the other hand is a *non-spiritual* form of arguments, derived from a more scientific frame, based on notions of systems and chaos theories. This argument refers to the interconnectedness of living organisms and ecosystems. The outcome of disturbing or manipulating such systems is unpredictable, and nature by definition avoids attempts to be controlled, it is characterized by self-regulation and non-mechanical patterns of behaviour; there is a delicate equilibrium that can be destroyed. Hence, biotechnology may disrupt nature’s mechanisms to maintain balance, leading to unintended and irreversible effects.

Regarding more recent developments in emerging technologies, in her analysis of ten years of public dialogues about science and technology in the United Kingdom, Melanie Smallman (2018) classified five classes of public discourses around various technologies (i.e., nanotechnology, geoengineering, synthetic biology), based on how the public draw on their previous experience of other technologies to guide their views on new developments. Of these classes, one is constituted by “technologies that work with the genetic building blocks of life, such as synthetic biology and GM [genetic modification]” (ibid., p. 658). Within this class, two factors are salient: the role of nature and shape of regulation. Regarding the former, Smallman suggests that the public uses three different concepts of nature or *naturalness*. The first, *ontological*, consists of a clear distinction between the state of being natural or unnatural, there can be no other states; natural is seen a more desired and acceptable state. A second factor is *ecological*, which (similarly to arguments above) considers nature as a balanced system that can be disrupted by man’s interference, with unforeseen consequences; the system’s integrity should be preserved. A third factor is *deontological*, setting a clear distinction between conforming to a natural order, or otherwise facing consequences; in this sense, ‘violating’ nature is seen as bringing negative outcomes.

As nature is a significant factor that shapes public views about technology, it is particularly a strong one for views on genetic engineering. A key take-away of Smallman’s work is that the importance of nature for the lay public is different than experts and policy makers, the latter being more optimistic about the benefits of science and the management of risks: what she associates with a sociotechnical imaginary of ‘science to the rescue.’ The public, she argues, indicates a ‘counter-imaginary’ of ‘contingent progress,’ which displays awareness about unintended consequences (or problems) caused by research, and its associations with industry and corporate interests, as well as matters of political economy.



### 2.3.5 Sociology of expectations

Sociology of Expectations bears common ground with sociotechnical imaginaries. The transformative power of science and technology point out to the future as an object subject to change and deliberation. Work in STS has conceptualized future as an ‘analytical object’ (Brown & Michael, 2003). Two aspects deserve attention: First, that the future through science and technology is created in the present (Brown, Rappert, & Webster, 2000), this provides a delicate sense of control over what will come. Second, throughout the literature it becomes apparent that also the past is drawn upon when making claims and constructing the future. For this field, the future is ‘contested,’ in the sense that there are many possible futures for every present, and actors want to forge it with their own technologies, securing a place in it (Brown et al., 2000). For Harro Van Lente (1993), promises and expectations about technology play an important role in shaping the trajectories of technology; the question then becomes what are the dynamics by which such technological change takes place, or what strategies use actors to mobilize resources and gain support to reify their visions. An example of a strategy is that of ‘self-fulfilling prophecies,’ suggested by Robert Merton (Borup et al., 2006).

Why are expectations so important in studies of technological change and innovation? Expectations serve to coordinate innovation efforts, or as Borup and colleagues (2006: 286) wrote, “Bridge or mediate across different boundaries and otherwise distinct (though overlapping) dimensions and levels.” They broker relationships between different actors and groups. Hence rhetoric, the discourse employed to inform, persuade, or motivate particular audiences, is employed to shape the future in significant ways. Van Lente (2000) in his study of the development of the High-definition television in Europe argues that promises play two roles: they give a sense of determination to a technology (i.e., the technology cannot be stopped), but also require that technologists work hard to make sure that technology actually happens. Furthermore, visions have two characteristics: they construct the future as desirable and positive, and deviate attention from the many technical problems faced by technologies (Sovacool & Ramana, 2015). Van Lente & Rip (1998) studied the dynamics of the emergence and stabilization of the membrane technology field as a form of ‘strategic science.’ Strategic science is better understood as a new category for policymakers, sitting in the interface of basic and applied research, where there is potential for application, but no immediate uses of a given technology. This creates an audience eager to hear about promises and invest in emerging technologies, in order to consolidate national agendas of global competitiveness and hence economic development. This in turn leads to the creation of a ‘rhetorical space’ in which promises are fully ventilated.

Eames and colleagues (2006) define expectations in terms of what they do, as “less formalised, often fragmented and partial, beliefs about the future”, and refer to *visions* as “internally coherent pictures of alternative future worlds. Normative in character, visions are explicitly intended to guide long-term action.” Something to note is that expectations are made along with *hype*, which is defined by Guice (1999: 84) as a ‘rhetorical strategy,’ acknowledging that it also bears an emotional component:

The most basic meaning of ‘hype’ in this context is ‘unwarranted and exaggerated claims’ which make an emotional appeal to the audience. In this usual sense, ‘hype’ is a mudslinging term, used to discount statements which the speaker does not support. However, putting to one side the issue of the truth or appropriateness of specific claims, it is possible to step back and recognize that hype can also be defined as a particular rhetorical strategy.

The above discussion on the expectations and promise is useful because these categories serve similar purposes to narratives and discourses, they have performative power. One of the main arguments I present is that xenobiologists need to gain visibility for their field in order to attract resources and prestige, and for doing so, they make the case that xenobiology can fulfil the promise of biocontainment and put forward narratives of exploration and navigation that may seem as transgressive. In this sense, it is possible to go in more depth to suggest that the way promises and solutions to problems are framed reflect particular configurations of society and tasks of science in society.

## **2.4 Laboratory, experimentation, society and the real world**

In this thesis I argue that governance frameworks could benefit from thinking of xenobiology as a form of social experimentation. Gross & Krohn (2004: 38) claim that for genetic engineering, “The question as to whether the risks of releasing GMOs are acceptable can only be answered by releasing them.” Deconstructing this sentence requires first to provide an overview of laboratory studies in STS, as well as what has been proposed as a distinction between experimentation in the laboratory, and in society or the real world. The advancement of emerging technologies raises the question, as a technology scales up, how are potential risks or consequences anticipated and tested in the real world? Xenobiologists promise to develop biocontained and safe genetically modified organisms that can be released into the ‘real world.’ In doing so, there is a fertile ground of meanings and attitudes between the life sciences and society as to what research is legitimate to be conducted, what are the limits and responsibilities of scientists, and what are the boundaries between the laboratory and society; and as I show in the next chapter, the boundaries between life and alternative forms of life. Furthermore, much of my data for this study was gathered from ethnographic observation in a xenobiology laboratory, building on previous work in STS over why the laboratory is a fruitful place for the study of scientific activities.

### 2.4.1 The laboratory and experimentation

STS has directed attention to the practices of the laboratory, and the conditions under which knowledge is produced. Inquiring over how 'facts' are constructed, Bruno Latour & Steve Woolgar (1979) were pioneers in suggesting that the laboratory is a place where 'mistakes' can be made, and where inscription devices are used to produce a written output (texts, papers) that limit counter-arguments, hence producing scientific facts; for them, science can be understood as a circulation of knowledge embedded in scientific articles. Other early laboratory studies have studied the laboratory as 'internalist' and 'externalist' perspectives and methods, or micro and macro (Knorr-Cetina, 1983), where nothing extraordinary and nothing scientific was happening inside the sacred walls of these temples (Knorr-Cetina, 1981). Other approaches have focused on anthropological analysis of laboratory culture in high-energy physics (Traweek, 1988), or laboratory science as shop work (Lynch, 1985). More recently, authors have challenged accounts of the making of scientific facts or deconstructing how truth claims. Park Doing (2008) argues laboratory studies have left these incomplete explanations because the 'facts' that laboratory studies follow seem to be settled by external sources.

The laboratory is important as a place where experiments are conducted. Scholars have revived attention in history and philosophy of science from theory to experimentation, aiming to understand what is unique about experimentation as a learning strategy (Hacking, 1983; Pickering, 1995; Rheinberger, 1997).<sup>38</sup> It has been assumed that the laboratory is a confined setting from the outside world, where knowledge is produced and experimentation takes place. The laboratory as an institution and a physical space has undergone transformations over different regimes of scientific research. For instance, the notion of the laboratory as a closed setting within which experiments are carried under controlled conditions was not present in seventeenth century England. Instead, experiments took the shape of performance, where the type of witness and trust in the experimenter were important criteria for assessing reliable knowledge. Experiments were conducted in private (as experiments in the making) and in public spaces, where they functioned as displays of already tried and tested procedures (Shapin, 1988).

More than a specific and delimited space, the laboratory for Guggenheim (2012) represents the division of a space with a controlled inside and an uncontrolled outside. Control refers to data and objects behaving within parameters that the experimenter

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<sup>38</sup> For attention to processes of experimentation, see Galison, 1987; Gooding, Pinch, & Schaffer, 1990; Lenoir, 1988.

determines. Such separation between inside and outside allows for two central features of the laboratory, according to Guggenheim, ‘placelessness’ and ‘consequence-free research.’ Placelessness refers to the generalization of epistemic claims made in the laboratory to non-controlled environments; what happens in the laboratory is meant to be independent of conditions (i.e., the environment) found outside, which should ensure reproducibility. Laboratory-made facts are considered true to everyone, anywhere.<sup>39</sup> Referring to the institutionalization of knowledge production, Arie Rip (2011) argues that a key characteristic of science is the creation of protected spaces, where experiments can be conducted under restricted conditions (I return to this theme in **Chapter four**, where I analyse safe spaces for experimentation in xenobiology). This allows for the exclusion of interference and unwanted visitors, and reduction of variety, to be productive. Such spaces enable and constraint, and their protection is a functional requirement for science. At the meso-level, protected spaces are created and maintained by sponsors, such as funding agencies; for the micro-level, such spaces comprise laboratories and controlled experiments. In Rip’s diagnosis, protected spaces are opening up to allow more interaction between science and society and allow plural knowledges to be seen as legitimate sources of knowledge production. Experimentation beyond the laboratory, that recognizes the social character of learning through experimentation, can be thought of as a recent phenomenon, but it is deeply rooted in the history of science. Approving the experimental method would turn society itself into an experiment. Although experiments could bring risks, they could also bring rewards and gains (Gross & Krohn, 2004).

The laboratory is special for Callon and colleagues (2009) because it is a place where the ‘research collective’ gets work done and knowledge is produced. They remark the collective nature of knowledge production that involves humans and nonhumans, particularly instruments and inscription devices. The authors refer to a third form of organization of research, in which researchers have ‘secluded’ in their laboratories, effectively imposing a break between the laboratory and the world, sheltered from the public, isolating potential interferences to experiments. The worlds created in the laboratory need to be taken back to society, which they call a ‘third translation’, or *‘laboratorization.’* According to the authors, the three stages are the following:

The first is that of the reduction of the big world (the macrocosm) to the small world (the microcosm) of the laboratory. The second stage is that of the formation and setting to work of a restricted research group that, relying on a strong concentration of instruments and abilities, devises and explores simplified objects. The third stage is that of the always perilous

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<sup>39</sup> For instance, Kohler (2002: 191) writes, “The simplicity and sameness of labs helps ensure that experiments turn out the same wherever they are done, which is one of the main reasons why we trust experiment more than other ways of knowing.” See also Kohler (2008).

return to the big world: Will the knowledge and machines produced in the confined space of the laboratory be able to survive and live in this world? (ibid., p. 48).

Callon and colleagues propose these stages to understand the origin of the strength and effectiveness of secluded research. For secluded research to take place, the chains of translations that allowed research to happen (and new knowledge to be produced) must be held together. This is partly facilitated by a proliferation of laboratories in society and the authority that comes along with them, what they call the 'laboratorization of society'. This question constitutes the bulk of the study of Bruno Latour's study (1983, 1988b) on the ground-breaking development of a vaccine for anthrax in cattle by Louis Pasteur, the domestication of a *Bacillus*. Pasteur succeeded in capturing the interests of other actors (like farmers) who otherwise would have no relation with the laboratory, by becoming an *obligatory passage point* (cf. Latour, 1987). Latour is not interested in notions of inside/outside the laboratory, or micro versus macro-sociological studies, but the ability of Pasteur to transform French society through his actions in the laboratory. Latour argues that the power of the laboratory lies in dominating asymmetries of scale, differences of scale are made irrelevant. The crucial aspects of the world are reconstituted in the laboratory, according to parameters established by researchers and the recalcitrance of objects.

Nevertheless, Matthias Gross (2015) argues that the laboratory is not the privileged location where knowledge production takes place. He turns around Latour's metaphor of the laboratory as a lever to transform society, suggesting that "the experimental processes taking place *in* and *with* society should be considered the normal, or the real-world, experiment. Thus, experiments in the real world are, in a sense, the real and true experiments, and the laboratory experiment is a temporarily postponed variant of it." (Emphasis original) (ibid., p. 4.). For instance, in the case of geothermal drilling, experimental practices such as where to take measurements or where to drill, take place before the experiment is brought into the laboratory.

Bringing laboratory research (or secluded research) back to the world is particularly difficult, according to Callon and colleagues (2009), who add that the process requires maintaining connections with the wild (or world), in terms of framing problems and considering complexities of the world (or scaling up). This leads them to argue that the division between the laboratory and the world is not only spatial, but also a division between experts and laypeople. They defend the relevance of involving the public in decision-making about science and technology, recognizing their *de facto* role as researchers in their own domains, or co-researchers, as they put it. Besides having a say in research agendas, co-researchers also ensure a plurality of outcomes from technoscience, recognizing that agents can make choices about the worlds that technoscience shape.

Consequence-free research, according to Krohn & Weyer (1994), allows the isolation of laboratory activities from consequences in the real world, or put otherwise, what happens in the laboratory stays in the laboratory. Actions in the laboratory should in principle pose no danger or risks to the outside world. The authors, who have played a major role in establishing the concept of '*real-world experimentation*,' also note that legitimization, or acceptance from society,<sup>40</sup> is needed in cases where scientists extend their research activities and related risks beyond the limits of the laboratory (which for them are not only physical, but institutional). As society becomes exposed to the risks of research, this involves a redistribution of responsibility. Traditionally, contemporary science draws on an institutionalised, free research arena for the production of knowledge. This is based, importantly, on "the assumption that theoretical statements and conclusions, as well as success and failure in experimentation, are free from moral considerations" (ibid., p. 174), which trace back to the ideas of Francis Bacon. For this to be preserved, they explain that two conditions must be met. First, activities in the laboratory must have no consequences outside the laboratory; and second, theoretical claims made in scientific circles must have no effect on everyday discourse outside science. Furthermore, Gross & Krohn (2004: 40) identify a series of institutional conditions and epistemological axioms that Bacon proposed for accepting experimental science. First, new knowledge (and its risks) is concealed by scientists until they determine its usefulness. Second, as science inherently involves errors and failures, these should take place in the laboratory and not in society. Third, 'scientific results' lead to the manipulation of the material world (i.e., magnetism, colour). Fourth, the experimenter performs experiments without being changed by them, or the objects and artefacts involved. According to the authors, these axioms have acquired a contractual basis, and constituted what has been called the social contract for science (cf. Guston, 1999).

A counter-paradigm to Bacon's idea of scientific practice was proposed by Johann Wolfgang von Goethe (Gross & Krohn, 2004), who thought of experimentation as a "mutual process of shaping the observer and the observed field of study" (ibid., p. 40). For him, phenomena influence other phenomena, making it impossible to isolate materials and effects in a laboratory, in contrast with Bacon's view of nature. Goethe privileged the lived experience of the researcher, in a process of mutual forming of subject and object. Without entering into details, Goethe provided a different interpretation of the experiment, which did not favour dominance over nature, and has resulted in fruitful non-laboratory fields of research. Another view of experimentation was also developed by the organic chemist Justus von Liebig (1803-1873) who considered the availability of world-wide agricultural resources,

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<sup>40</sup> This is related to the distinction between *context of discovery* and *context of justification*, or put simply, what is discovered in the laboratory needs justification to be used outside of it. See Schickore & Steinle (2006).

or a 'chemistry of the world,' and its connection with economic and cultural change, emphasizing lessons from the complexity and non-linear dynamics of nature.

Based on the legacy of the Chicago School of Sociology, Matthias Gross & Krohn (2005) draw attention to the experimental character of temporary society; experimentation not only takes place in the confined boundaries of the laboratory, but also in societies. For the Chicago School, which considered Chicago as its laboratory and subject of study, the modern city and thus modern society in general were understood as a partial natural phenomenon. In particular, for urban sociologist Robert Park, the city (and the society it sustains) presents its own dynamics, which are dependent on the material environment; experiments already take place in society and are "performed by society itself" (ibid., p. 77), as an open-ended experiment. The processes behind the development of the city and of society at large would allow a better (experimentally) understanding of how society works. For Park the city serves as the habitat of man, which changes man as much as it is changed by society.

#### **2.4.2 Risk & uncertainty**

For this thesis, the constructed character of biosafety in xenobiology depends on notions of experimentation, risk and uncertainty. The experimental aspect of technologies and the many scenarios that appear from emerging and new technologies, create a need to examine elemental concepts, such as the notion of hazard often used to indicate that a technology, or its use, can cause damage or otherwise undesirable effects. The term risk can be seen as a specification of the term hazard; an often-used definition of risk is the product of the probability of an undesirable event and the impact of that event. A requirement to express a hazard within a risk requires knowledge of the potential consequences of a technology, the impact of those consequences and the probability of their occurrence. Uncertainty refers to a situation in which what might go wrong is known, but knowledge to express a hazard within a risk is absent. Ignorance refers to the situation in which we do not even know what could go wrong, resulting in unknown hazards. In some cases, potential hazards cannot be expressed in risks because their occurrence depends on the behaviour of users or operators. Such situations may be characterized as indeterminate because the causal chains potentially leading to a hazard are open and depend on the actions of some relevant actor (Wynne, 1992). STS analysts have disputed that there is a single, if complex, phenomenon called risk, generally defined as:  $risk = probability \times magnitude / time$ . This conception of risk is misleading for 'societal risk management' (Rayner & Cantor, 1987). For the public acceptance of risk, people usually do not think about probabilities, and the probabilities are very low for the type of accidents or unintended consequences that can result from new technologies. Rayner and Cantor argue for a change of perspective, from 'how safe is safe enough,' to the question of 'how

*fair is safe enough?*' this allows broadening discussions about risk, to incorporate principles like trust, equity, liability and consent. At stake is decision-making in conditions of ignorance, rather than developing better predictions and aiming to *know* all possible unintended consequences (Collingridge, 1980).

How to understand such predominant framing of science and technology around risk? Brian Wynne (2002) criticizes that debates over emerging technologies have locked into an instrumental discourse about risk; this is the consequence of a realist framing, which "excludes more reflexive questions about the human purposes and visions which shape front-end innovation commitments" (ibid., p. 463). Welsh & Wynne (2013) add that scientific institutions have established the authority to frame issues around risk, in ways that are beyond the role of science of providing the best information and facts available.

Few authors have been as influential as Ulrich Beck in our thinking about risk as a social and man-made phenomenon. His renowned 'risk society' thesis (Beck, 1992) comprises that the risks that society faces no longer derive from (pre-industrial) natural hazards, but are the result of unintended consequences of modernization itself, most notably in the form of climate change produced by human activity, or nuclear power accidents. Such risks are unconstrained by time and space, affecting most people equally.<sup>41</sup> Beck draws attention to the inadequacy of institutions to deal with risk, which are also to blame about the manufactured nature of risks that we face; their exposure to risk debilitates their public authority. Moreover, similar to Bruno Latour, Beck claims that nobody is responsible for the uncontrollable consequences of technology, raising a problem of accountability. Uncertainty for Beck also permeates individual identity, as lives of individuals are no longer shaped according to collective structures, but their own circumstances and decisions. Gabe Mythen (2005) summarizes Beck's ideas on work relations, which comprise that risk has consequences for the relationship between the individual, society, and work practices such as labour markets, employment contracts and modes of production-. This means less job security, and less availability of jobs, in a globalized world where highly qualified workers can move around as they are required to. Cultural, historical and regional differences still matter if the risk society thesis is taken seriously.

Similar to the 'risk society' thesis, we are in a world where high-risk technologies have become ubiquitous, shows Charles Perrow (1984), who proposes that accidents resulting from technology have become 'normal', in the sense of being an inherent and inevitable property of technological systems. This is due to unexpected interactions between

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<sup>41</sup> This point of the logic of distribution of risks is contested, since Beck privileges a logic of risk rather than a logic of class. After all, risk impacts individuals differently depending on their socioeconomic status.



components (or failures) of ever more complex systems. Perrow's lesson is that for preventing normal accidents, relying on technofixes is not a feasible solution, since they make systems more complex and interconnected. Indeed, more technological complexity can introduce new accidents into a system, and act as excuses for poor organizational or managerial practices, or in the case of 'safety devices', deceive or provide the illusion that inevitable failures have been controlled appropriately. Commenting on the Chernobyl accident as part of an ongoing experiment with nuclear power technology, Krohn & Weingart (1987) criticize risk assessment approaches, because they fail to acknowledge social factors in the judgements and models about risk. In their analysis they warn against the construction of an illusion of safety, as absolute testing is not achievable for technologies like nuclear energy. Such an illusion plays a role in keeping fears of the public under control. Public acceptance comes into question when the experimental nature of new technologies is revealed, putting into question the authority of governmental institutions to handle controversies and measure risk, which can lead to weakening institutional credibility.

Perrow (1984) also elaborates on the catastrophic potential of DNA, not due to the tight coupling of interconnected components, but the opposite, the potential to create interactions between systems that were not previously linked: links that cannot be foreseen. Once the linkage is made, it cannot be controlled by operators. In addition to systemic accidents, Perrow (1984: 294-301) warns against ecosystem accidents. In these cases, risk cannot be calculated in advance and the initial event becomes linked with other systems from which it was believed to be independent. Knowledge of the artificial material that may have caused the initial event is limited. According to Perrow, this is due to the "inadequate definition of system boundaries" (p. 296), between artificial and natural systems. Simply put, as humans harvest the power of nature, they make artefacts or technologies that rely on natural systems, which are not fully understood.

In what follows, having provided an overview of ideas on experimentation and the boundaries (or lack of) of the laboratory and risk and uncertainty, provides a basis to discuss further some of the main theoretical tools I employ in this thesis, 'real-world experimentation' and 'collective experimentation.' In essence, both tools invite us to think about risk differently, and the lack of certainty leads to acting cautious and caring.

### **2.4.3 Real-world and collective experimentation**

In this thesis I combine elements from STS like co-production and sociotechnical imaginaries with other strands of the literature of sociology of risk and STS like real-world experimentation and collective experimentation, due to their importance in thinking about

the dichotomy between safety and risk, or control and uncertainty. For Gross and Kohn, experimentation is more than simple trial and error; it includes embracing ignorance. The framework of real-world experimentation highlights the importance of uncertainty in debates over science and politics. A tenet of this framework is that scientific research in late modernity is increasingly erasing the boundaries between the laboratory and society, after observing that scientific processes have been released into society at large, whether intentionally (as in genetic engineering), or accidentally (as in Chernobyl nuclear plant explosion). Common to these processes is that experimenters and operators lack complete control, and entertain an illusion of control in order to ensure that research activities last (Gross, 2010a). Real-world experimentation warns us that the experimental method in the laboratory is extended to the public, which implies that the public is subject to the risks of these experiments. Nevertheless, this is unavoidable. The growth in complexity that is characteristic of high technologies dictates that in many respects, learning about risks and benefits can only be achieved by implementing such technologies. Thus, as Gross & Hoffmann-Riem (2005: 270) note, reflecting upon ecological restoration, “The problem posed by ecological risks cannot be solved with certainty on the basis of traditional experimental (field) methods.”

Nevertheless, more than a set of principles, or an analytical lens, I interpret real-world experimentation as an inclination toward embracing uncertainty in scientific processes. More specifically, real-world experimentation is about design principles, or strategies. For example, the careful development of a design that minimizes stress and unexpected reactions is a precondition for the implementation of a technology or ecological intervention. If something goes wrong, all the effort is focused on keeping the installation running and the hazards down. Learning focuses on the local conditions to keep an installation going, not on finding the parameters of a general solution (Krohn, 2007). A case in point is provided by Gross & Hoffmann-Riem (2005), who draw lessons for real-world experimentation from ecological restoration,<sup>42</sup> based on the case of project of restoring a landfill in Chicago (Montrose Point). Highlighting the role of surprise and that the latter framework occurs in cycle, emphasizing involvement by experts and lay people at the same level. Ecological restoration opens up new ways in which scientific practices can be understood when they occur in the real world, providing an enlarged definition of “scientific research” that has promoted public involvement in science. In its cyclical component, experimentation and learning are understood as an ongoing process, based on recursive loops.

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<sup>42</sup> The practice of renewing and restoring degraded, damaged, or destroyed ecosystems and habitats in the environment by active human intervention and action.

Real-world experimentation shares elements with ‘collective experimentation,’ as both highlight the experimental character of technological innovation, and the need to give up control. Collective experimentation is a term coined by Bruno Latour (2004) in his book *‘The Politics of Nature,’* a reimagination of technical democracy. In the book he extends the question of democracy to nonhumans, and rethinks public institutions. It is an effort to do away with the ‘old constitution’ associated with modernity that has been constituted by two (separate) houses: society as an assembly of humans, and nature as an assembly of things (or nonhumans). Latour suggests to overcome classic concepts like nature and society, replacing the notion of the social, for a sociology of associations (cf. Latour, 2005). The associations of humans and nonhumans still need some form of representation, so the task of ‘political ecology’ is one of representation, of how the multiplicity of non-humans become associated. In this way, the constitution that Latour proposes is a platform for distributing forms of speech; it is the only way to compose *a common world*.

Replacing the old constitution would result in Latour’s collective. However, Latour does not specify how the collective is different from the common world, and what are the boundaries between collectives, or their scale. The collective, composed by both humans and nonhumans, does not mean that everything goes, or that everything should be included. Precisely, collective experimentation is the process of *assembling (or convoking) the collective*, testing what can constitute it. To understand the collective, it is crucial to point out how it relates to categories that Latour wants to get rid of; for instance, he writes:

The historical importance of ecological crises stems not from a new concern with nature but, on the contrary, from the impossibility of continuing to imagine politics on one side and, on the other, a nature that would serve politics simultaneously as a standard, a foil, a reserve, a resource, and a public dumping ground (ibid., p. 58).

He further clarifies that

I use the word only to mark a political philosophy in which there are no longer two major poles of attraction, one that would produce unity in the form of nature and another that would maintain multiplicity in the form of societies (ibid., p. 59).

Important for our understanding of risk and uncertainty in xenobiology, Latour (2011) associates collective experimentation with an understanding of the precautionary principle as giving up the possibility to fully anticipate consequences. He writes the following (p. 12–13):

The precautionary principle means exactly the opposite of this abstention. It is a call for experimentation, invention, exploration, and of course risk-taking. ... The more risk we take, the more careful we are. This is how we describe an experience and what an experienced man or woman is. Well, what is true of daily experience becomes now true of the collective experiment as well, thanks to the precautionary principle.

The collective that Latour advocates for results in exclusion, as not everything would be considered. Even though Latour develops the concept in a theoretical and abstract fashion, for our purposes the message we should take home is that collective experimentation involves

composing the common world through conducting series of trials, documenting the results, and employing them for the next iteration (in a form of feedback that is part of a *learning curve*). This separates Latour's political ecology from modernism, whose overconfidence in absolute knowledge yielded propensity to unforeseen catastrophes. In fact, Latour's political ecology could be understood as a rejection of hubris from scientists, a recognition that the advancement of science will not contribute to ending uncertainties (and hence controversies), but to their proliferation. To close this summary of Latour's collective experimentation, it is worth providing his account of what experimentation consists of. Experimentation in this context refers to the work of collecting 'the collective' into a whole, of recruiting an assembly. In Latour's words:

Experimentation on what? On the attachments and detachments that are going to allow it, at a given moment, to identify the candidates for common existence, and to decide whether those candidates can be situated within the collective or whether they must, according to due process, become provisional enemies. ... the entire collective has to inquire into the trials that will allow it to decide whether it is right or wrong to carry out that addition or subtraction (p. 196).

Collective experimentation also concerns matters of scale. This is best exemplified by global warming, geoengineering, or 'gene drives,' in which boundaries (e.g. between nations or regions) are no longer meaningful (Latour, 2011). A corollary of collective experimentation is that no one is in charge of such an experiment, and no one is explicitly responsible for monitoring them (*ibid.*). Matthias Gross (2010b) draws parallels between Latour's collective experimentation and the practice of ecological design and restoration. He points out the need to 'operationalize' the concept and its usefulness for the social sciences depends on the concept being free from abstract conceptions and metaphors. The concept, as articulated by Latour, risks being lost as a difficult language to refer to 'difficult and unusual processes of participation' (*ibid.*, p. 68). This direction requires we shift our attention to experimental designs for the real world, although Gross recognizes Latour's attention to a protocol for experimentation (*cf.* Latour, 2001). A design, according to Gross, should include:

The continual renegotiation of the course of the experiment among heterogeneous actors, including nature as an actor; the inclusion of—potentially all—citizens as active co-designers and co-researchers; and, finally, a process in which surprising events (whether perceived as natural or as "social") are processed in such a way that they lead to new knowledge about natural or "social" phenomena that will be useful in the future (Gross, 2010b: 69).

In addition to recognizing the importance of talking about collectives, Gross recaptures Latour's collective experiment in terms of the already discussed real-world experimentation. So, what do we gain from overlapping these two concepts? In real world experimentation, Gross argues, the distinction between established facts (i.e., the law of gravity) and 'new facts' —facts that surprise and whose causes, effects and meanings are still subject to contestation for members of the collective— that Latour proposes are unnecessary, since

surprises are understood as deviations of what is expected, and they depend on an attribution that depends on an observer (judgment/evaluation). In real-world experimentation, values and surprises (new facts, or non-knowledge) and whether to continue an experiment despite newly obtained knowledge, should be negotiated by the actors involved.

So far, I have discussed real-world experimentation and collective experimentation in abstract terms. In what follows, I trace connections between such frameworks and emerging technologies, such as genetic engineering. Concepts like real-world experimentation or collective experimentation have not been widely adopted to think of governing of emerging technologies as experiments that transcend the laboratory to involve society. Jack Stilgoe (2015, 2016) provides a reflection of the geoengineering experiment SPICE (Stratospheric Particle Injection for Climate Engineering) that aimed to test a tethered helium balloon a kilometre up in the sky with a hose attached. For Stilgoe, the experiment is also a social experiment, where the imaginaries and uncertainties of geoengineering are produced and contested, putting to the test the legitimacy of geoengineering. Conceiving SPICE as a ‘social experiment’ helps to identify and reflect what is at stake in geoengineering research. He proposes a shift in thinking about governance of geoengineering, from a regime of technoscientific promises to one of collective experimentation (Joly, Rip, & Callon, 2010).<sup>43</sup> Joly and colleagues identify as key features of a regime of collective experimentation, a different division of labour from the dominant one that establishes technology promoters and enactors on the one hand, and civil society on the other hand, a commitment to try various technological promises and paths, and a wider participation of actors that enable new forms of interaction between scientists and other actors.

In rethinking geoengineering within a regime of collective experimentation (Stilgoe, 2016), Stilgoe suggests that uncertainty is inevitable and expanding, as opposed to soluble through research. It also extends to uncertainties of implications, feasibility and design. Experimentation is seen to include science in society with the relevant aspects it brings along like politics and publics, and “research and deployment are entangled in the same social experiment” (ibid., p. 864). Also relevant is the inclination to reflexively question the characterization of problems deemed to be solvable through research, and the recognition of ‘entanglements’ as a core feature of governance. Stilgoe’s work employs experiments and *design* of new technologies as sites to think about what is at stake, or as Stilgoe puts it, “The scrutiny of experimental intentions and the imaginaries that sit behind them” (p. 865).

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<sup>43</sup> Joly et al. 2010 refer to a regime of innovation as a paradigm, a notion of how things should be done. It involves distributions of power and agency, social relations, roles of actors. See also Felt & Wynne (2007) for an overview of regimes of innovation, in particular, collective experimentation, and its association with risk, master narratives and imaginaries.

Referring to the hazards of nuclear power, Ibo van de Poel (2011) asks about the conditions under which experiments with nuclear energy technology (and by extension, emerging technologies) are or might be acceptable.<sup>44</sup> Conceiving technologies as a social (or collective) experiment is not free of criticism. As a metaphor, technology as a social experiment does not do enough in figuring out whether new technologies are ethically acceptable, and its role is mostly delaying decision making (Peterson, 2017). This line of criticism, however, misses the point of real-world experimentation, in the sense that once we accept that the deployment of technologies is not restricted to the laboratory, this expands the range of actors affected (or who have stakes) by the technology, who should have a say in its progression, expands. When this dynamic involves uncertainties and the certainty of surprise, adaptive and flexible approaches are required, which help reflect power relations among different actors, and question the framing of problems that technologies aim to solve. In terms of ethics, the question of acceptability hosts a plethora of concerns, including risks, matters of design, and the distribution of responsibilities (van de Poel, 2013).

STS scholars have proposed to increase public participation in the development of emerging technologies, which would provide gains in rationality, based on the idea that laypeople possess alternative rationalities and moral compasses that should be taken into account in controversial scientific-technical debates (Wynne, 1996a). Sheila Jasanoff also supports public participation, for instance by formulating “public engagement is needed in order to test and contest the framing of the issues that experts are to resolve. Without such critical supervision, experts have often found themselves offering irrelevant advice on wrong or misguided questions” (Jasanoff, 2003: 397-398). Building up on real-world experimentation as a shift in which practices of knowledge production that used to take place within the confined setting of a laboratory are expanding to encompass the whole of society, Bogner (2012) suggests that a turn in public participation acquires the form of a laboratory experiment. This is because public participation exercises are organized top-down under methodologically controlled designs by a team of researchers who observe the unfolding of the interactions among participants. Thus, no gains in ‘rationality’ are obtained, and participation hardly achieves political consequences. For our purposes, it is noteworthy the argument that both the topics for deliberation and participants of discussions are determined in advance, resulting in an abstracted, contained social world that does not necessarily reflect the views of public concerned with emerging technologies.

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<sup>44</sup> Van de Poel argues that in addition to ensuring technical sufficiency, by means of containment, monitoring, scaling up and the possibility of stopping the experiment, conditions for experimentation should include democratic decision-making and legitimation, and considerations of ‘distributive justice.’

Callon and colleagues (2009) embrace the role of controversies to explore framings and problems of different domains in heterogeneous open (public) spaces that they call 'hybrid forums,'<sup>45</sup> as a form of 'dialogic democracy.' These spaces would allow collaboration and discussion among technical experts and, politicians, laypersons and so on, on shared matters of concern. Discussions in these forums centre around the shared exploration of possible worlds and scenarios, allowing learning about the interests and preoccupations of different identities that are formed in the forums. Forums do not seek consensus, but an open exploration of concerns with publics that existing democratic institutions have failed to represent.

Related to decision-making under conditions of ignorance and uncertainty, Overdeest, Bleicher, & Gross (2010) build upon the work of American pragmatists to develop experimental policies. They argue that for American pragmatists, meaning and reason were social in nature, which led them to value communication and deliberative approaches for democracy. This in turn the authors argue inspired Habermas (1987) to develop his ideas of the public sphere and communicative rationality. In this view, decisions reached by a community would be legitimate if they were the outcome of discursive opportunities, in which actors challenged each other's reasons based on the best arguments. Overdeest and colleagues (2010) argue that in environmental matters some actors may not have sufficient power to be heard. More importantly, participatory governance approaches, like those developed by Habermas, are not well suited for 'real world' decision making, because they do not deal with uncertainties. Public participation is not sufficient and actors cannot agree on what is unknown in the present, which cannot be remedied by more scientific evidence. The authors write (p. 282):

It is clear to most practitioners that scientific knowledge, as well as research, in general is always limited by human ignorance, which makes reliance on science in new forms of governance important, but nevertheless tricky, since the actors involved, in order to be able to act, need to agree on what is not known and take it into account for future planning (emphasis original).

In summary, real-world experimentation involves a shift of a philosophy of science policy that emphasizes public involvement in the development of new technologies, and collective learning. As Matthias Gross & Wolfgang Krohn (2004: 48–49) write, "formulating a new contract between science and society that makes science more public and members of the public more ready to engage in knowledge production relevant to shaping their lives, communities, and environments."

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<sup>45</sup> For the original formulation of the concept of hybrid forums, see Callon & Rip (1991).

#### 2.4.4 Safety by design and biocontainment

Few studies in STS have paid attention to the constructed character of safety, including studies about safety practices in the laboratory (Sims, 2005), or risk assessment and regulation (Bijker, 2007; Jasanoff, 2005a). In his study of the making of a safe innovation, the application of ice structuring protein (ISP) in ice cream, Penders (2011) shows that different types of safety co-exist and compete, are constructed and negotiated. Safety goes beyond the characteristics or properties of a product, as it is relational to scientific considerations (like the mode of action of a protein), as well as social aspects such as regulation and public opinion. More than the absence of risk, safety is an attribute that is incorporated into a product.

Most remarkably from Pender's study is the notion of safety as associated with public perceptions of food and genetic engineering. As he writes, "safety" has very little to do with regulations or toxicology. It is about safe investment and safe use of resources, about positioning a product in a society critical of GM technology and technological foods" (ibid., p. 476). In xenobiology, through built-in-safety it is expected that 'public safety' is achieved, but this is supposed to work according to the scientists in the field based on their view of how society works and how they construct fear and risks. Penders also shows that contested terms as 'artificiality' (as a high-tech protein ingredient) can be a threat to public safety of innovations, this can be managed. For instance, Unilever decided to choose a particular expression system for the ice-structuring protein, such as the baker's yeast, which would be more familiar for the public.

Designing for safety and minimizing risk is not new, it has been embraced in engineering (i.e., Brown, 1976; Wang et al., 1995), and has gained credence in nanotechnology circles, particularly as a property to be incorporated in new materials (Costa, 2016; Fadeel, 2013; Geraci et al., 2015; Morose, 2010; Riediker, 2011; Truong, Simonich, Sali, & Tanguay, 2012). Lessons from the field of 'drug discovery and development' suggest that safety by design should be considered the starting point rather than the end point when it comes to developing safe products for health and the environment. However, it cannot obviate the need to assess risk (Hjorth, van Hove, & Wickson, 2017). Safety-by-design highlights questions about what is safe enough, and who gets to define acceptable levels of safety.

In an introduction for a special issue on safety by design in nanotechnology, Schwarz-Plaschg, Kallhoff, & Eisenberger (2017) make relevant points for this study. First, they criticize that safety has become instrumentalised as an enabler of innovation (or as a way to overcome regulatory obstacles). Second, instead of assuming safety can be a property of materials or products, for the authors safety is a relational category: what is considered safe or unsafe depends on its relation to other entities. A third point takes issue with the linear



model of innovation. They write, “the linear innovation approach of these models implies knowledge that is not existent at certain stages and also does not take into account that research and innovation processes may better be conceptualised as non-linear collective and iterative learning” (ibid., p. 278). For them, safety-by-design is a cumulative process, in a product development pathway, in which different actors interact and are responsible for meanings of safety.

Safety-by-design has implications for democratic governance that I examine about xenobiology in this thesis. Van de Poel & Robaey (2017) criticize safety-by-design for being undemocratic and designing out *indeterminacy* (that the safety of a technology depends on the behaviour of actors in the value chain, like users or operators); they argue that this decreases, rather than increases, the ability to deal with unexpected or unknown risks. At the same time, safety-by-design negates a role for actors or users in achieving safety, and results in less flexible designs. A key set of questions related to governance is about what actors are responsible for addressing the risk of new technologies or ensuring their safety. For Robaey, Spruit, & van de Poel (2017), assuming from the start that researchers bear special responsibility for safety raises particular issues.<sup>46</sup> First, they see as problematic the assumption that safety issues can be addressed and controlled in the R&D phase, which predicates that such type of issues can be known in advance, without considering how artefacts or materials may be used. Second, they ask if other actors should assume blame if things go wrong. They extend responsibility to ownership of technology, even though owners may not be fully aware of the consequences of a technology. In this sense, they write, “Owners have to act as responsible experimenters” (ibid., p. 17).

Christopher Kelty (2009) describes the story of how ‘safety-by-design’ was positioned in nanotechnology as a practice of responsibility. He argues that concern of toxicity of new nanomaterials was not a concern for scientists and was raised by scientist Vicki Colvin who aimed to convince her peers that safety should be a property of nanomaterials and created a new mode of veridiction. The question became not whether materials are safe, but how safety as a value shifted the discussion toward how materials can be engineered to be made safer, and what type of data is required for this (such as toxicological data or chemical structures). For McCarthy & Kelty (2010), if risk is to be associated with responsibility, it must be formulated as a legitimate scientific endeavour, turning responsibility into something doable, addressable as a scientific problem.

Experimentation in genetic engineering has also been reported by STS commentators. The ideas of real-world experimentation have been adopted by European regulation on GM

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<sup>46</sup> In particular, the authors emphasize the distinctions between backward-looking and forward-looking moral responsibility.

crops (Levidow & Carr, 2007). These authors identify competing frames in the 1990s over the morality and hazards of GM crops for the socio-natural order, frames that oppose or promote agri-biotech. Of these tensions, the most important one was opponents of GM stigmatizing agri-biotech, considering it a form of pollution. As a result, regulators employed a step-by-step procedure to evaluate the impacts of GM crops, making the assessment process more relaxed and facilitating the commercialization of novel crops. Such practices extended the disciplinary boundaries of science to include modes of operator (farmer) behaviour and diverse agri-environmental conditions. Although decision makers expected to earn legitimacy for GM crops, while “keeping GM products on trial” (ibid., p. 28), experimentation practices that extended to discipline farmers led to further conflict, impeding the commercialization of GM products. In a study about GM trials in France, where over the years of ensuing controversy, attacks on field trials of GM crops became a way of challenging power structures of seed firms and government bodies (Bonneuil, Joly, & Marris, 2008). For the authors, the boundaries between science and society had been redrawn and remained unstable, noting that such boundaries are constantly renewed and the “product of boundary work carried out by actors in different interacting arenas” (ibid., p. 224). The act of destruction became a channel for public participation, although this was only part of reframing processes by various actors in different arenas.

Ideas on real-world and collective experimentation, and elements from sociology of risk, help to put together a conceptualization of the relationship between xenobiology and biosafety that I study in this thesis. Safety and risk can have many meanings depending on how actors articulate them, so this literature helps to orientate the study of these contested terms. More importantly, the works I have introduced question the boundaries between the laboratory and society, which I point is one of the main elements of novelty in xenobiology, its bold expansions of limits of what is doable to portray that safety is found at the boundaries of life. Not only the literature I have presented will help to articulate ways of thinking about xenobiology that downplay control and embrace uncertainty, but it will also help make connections between this literature and the other contributions in STS I refer to in this chapter. In what follows, I address important themes in the ethics of science and technology, which serve as elements to re-think values and meanings embedded in the artefacts of xenobiology.

## **2.5 Ethics, laboratory engagement & post-ELSI**

The literature on engineering ethics has addressed moral responsibility, typically focusing on questions related to liability and blameworthiness. Researchers have focused on the prevention of accidents and the allocation of responsibility, as well as establishing causal

relationships between engineers and the artefacts or sociotechnical systems they design. Engineering ethics and STS have not coalesced significantly, in part because of the externalist focus of the former and the (arguably) lack of normative discussion in STS (van de Poel & Verbeek, 2006). A critique of the engineering ethics literature is offered by Lynch & Kline (2000), who build upon STS scholarship. They argue that engineering ethics focuses on abstract moral theories or professional codes, and who bears responsibility. The authors write that

Engineering ethicists usually assume that the primary obstacle that engineers face in acting ethically in promoting public safety in organizations is amoral calculation—whether in themselves or in their managers. The trick then becomes to embolden the engineer to resist this amoral calculation, whether it be by an infusion of moral theory or by inspiring tales of moral heroism or by an emphasis on what professional codes of conduct require (*ibid.*, p. 199).

This leads to calls for ‘heroic figures’ or whistle-blowers, to prevent accidents from happening. For example Roger Boisjoly, engineer in the American corporation Thiokol who foresaw the Challenger accident of 1986. For them, ethical positions that consider individual action as the locus of intervention are not practical solutions to ethical dilemmas. The authors use the historical ethnography of the Challenger disaster written by Diane Vaughan (1996) as an example of an STS analysis of a case study that places emphasis on cultural understandings of risk in a complex engineering organization (like NASA) and the commonplace practices involved in engineering decisions. According to the authors, Vaughan’s analysis shows that anomalies, or deviations of the system’s expected behaviour are to be expected, and are what Vaughan calls the ‘normalization of deviance.’ In NASA’s culture, risk became incrementally acceptable. Lynch and Klyne argue, “early decisions may help legitimize later ones”, adding that “incremental change may lead to constructions of acceptable risk that would not have otherwise been accepted” (*ibid.*, p. 201).

A different stance is taken by Michael Pritchard (2001), who highlights the importance of engineer’s agency, or ‘character and imagination,’ rather than ‘social explanations.’ Pritchard argues, along the canon of engineering ethics, that among the duties of a good engineer is the protection of public safety, health, and welfare. For him, imagination is not about just fulfilling the duties as an engineer, but proactively anticipating safety concerns and daring to doubt the assumptions of an engineering design. It involves finding alternative ways of solving problems, relating to stakeholders and handling pressures. While I subscribe to Lynch and Kline’s criticism of the engineering ethics literature, their analysis focuses on the prevention of accidents or disasters in engineering. In this dissertation I am not concerned so much with the risks of xenobiology, but the broadening of the debate about the visions and possibilities of the field, and what conceptions it presents of the good life and the public

good. Such process has been addressed in the laboratory, with ‘big science’ projects like the Human Genome Project.

Cynthia Selin (2008) reminds us of the tensions associated with studying the future. Attention to the future is a key component of ‘anticipatory governance,’ where prediction is no longer the goal, but rather capacity for action (Guston & Sarewitz, 2002). Phil Macnaghten and colleagues (2005) proposed an agenda for the role of social scientists in technology development, following new opportunities and challenges that nanotechnology presents. They propose five potential areas of social research activity: *imaginaries, public engagement, governance, globalization, and emergence*. They suggest interrogating the role of imaginaries in the development of a field. In terms of method, they note:

Such research poses significant methodological challenges... To understand the nature, origins, and effects of such imaginaries, and to find ways of opening them to greater scientific reflection and public debate, will require informed interaction with scientific actors in their own “life worlds.” This implies a potential role for social scientist ethnographers as a new kind of actor-participant in those scientific knowledge communities (Macnaghten et al., 2005: 280).

This shift in governance also brings attention to the role of science in society, which in the case of Europe requires rethinking the balance of innovation versus societal needs, and how this contributes to the future of Europe (Felt, 2014). Noteworthy, Ulrike Felt draws attention to technoscientific maps that recreate realities of where science is conducted and by whom. The mere fact of representing world-making through maps is an exercise of reifying certain visions of technoscience. In this way, social scientists are called to yield visible what has been held invisible, or *monsters*.<sup>47</sup> Monsters may be understood as creatures coming before their time, unexpected, or as part of a wider reality unacknowledged by conventional world views. Felt indicates that the role of social scientists is to broaden views, or more precisely, to create space for ‘the monsters.’ This echoes with ‘matters of care’ (de la Bellacasa, 2011), in which attention is called to making visible ‘neglected things.’ Felt’s article is written in the context of Horizon’s 2020 vision of Europe as an *Innovation Union*. She argues that illustrating the benefits of science, in addition to economic gains, is neglected and needs visibility. This is also articulated in the approach to governance encompassed by RRI, characterized by aiming to orienting the ‘right impacts’ of a technology emphasis on stakeholders (von Schomberg 2013; cf. Owen et al. 2012).<sup>48</sup>

One of the pillars of RRI is ‘anticipation’ (Stilgoe, Owen, et al., 2013), of which an unresolved issue is *novelty* (Guston, 2013). Determining whether a technology is new and

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<sup>47</sup> Following John Law’s 1991 *A Sociology of Monsters*.

<sup>48</sup> Defining what are the right impacts is still a hot topic of debate, yet von Schomberg argues they could be about the Aristotelean notion of the ‘good life’. Nonetheless, the Lund Declaration of the European Commission (2009) provided a set of priorities about what these grand challenges may be.

brings novel challenges is a political act. For Guston, assessing novelty is not enough. He also asks about the ‘purpose’ of a technology: “The relevant questions are *why might it be done*, and if it is to be done, how best to do it. These are anticipatory questions” (emphasis original) (ibid., p. 114). In this regard scientists have a major role to play both in raising these questions and facilitating dialogue and the appropriate course of action.

### 2.5.1 The ethical, legal and social angles of new technologies

The social study of synthetic biology and xenobiology, as mentioned above, owes to an interest in shaping the outcome of research in these fields, given the high stakes in terms of ethical and political issues of disciplines in the life sciences. Before the execution of the *Human Genome Project* (HGP), there was caution in the community of social scientists about its potential negative implications –ethical, legal and social–, which were addressed by an ‘ELSI’<sup>49</sup> programme that received 3% of the total funding for the HGP, by the NIH (Cook-Deegan, 1994). The intention of the ELSI programme in bringing socio–ethical concerns into science and technology reflects a gap between social sciences and natural sciences, disciplines advancing at different speeds, with different interests. This can be seen as social scientists and natural scientists belonging to different cultures (Snow, 1961), with few (or none) shared goals or interests. Although ELSI became an innovation in bioethics and governance of the life sciences, receiving large funds (Meslin, Thomson, & Boyer, 1997), it has been criticised for not delivering its promise. ELSI researchers became too close to their “object of study” (Zwart & Nelis, 2009), did not pose objections to the unfolding of the human genome project (Fisher, 2005), and used the programme as a “cash cow for bioethics” (Powledge, 2003). ELSI dealt with the consequences of genomic research ‘downstream’ Rabinow & Bennett (2009). Nydal and colleagues (2015) argue that ELSA originally was formulated as an attempt to limit the negative consequences of biotechnology, instead of addressing the benefits of the field. Hilgartner, Prainsack, & Hurlbut (2016) portray ELSI and ELSA programmes as tools of governance and draw attention to the forms of power that these programmes constitute and exert, and their lack of reflexivity on their own power, for example in terms of determining what issues warrant deliberation and what controversies should be dealt with regulation. They add the following:

ELS[I/A] programs reflect and reinscribe traditional imaginaries of orderly science-society relations. These imaginaries often rest on views of the nature of science, technology, and society that STS problematizes, such as the fact/value distinction, the self-evidence of power relations, and asymmetrical explanation of the social causes of truth and error (ibid., p. 832).

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<sup>49</sup> The acronyms ELSI (in the United States) and ELSA (in Europe) refer to research activities that anticipate and address ethical, legal and social implications (ELSI) or aspects (ELSA) of emerging life sciences, notably genomics and nanotechnology.

A transition from ELSI to a different form of engagement is underway. A ‘post-ELSI’ turn is well exemplified in the manifesto of Balmer and colleagues (2012) in the UK. The authors express inconformity with the perceived role of social scientists in technology development and call for a revision of their relationship with natural scientists, providing more flexibility to the process and recognizing the symbiotic benefits of collaboration. The authors bring attention to ‘undertaking collective experiments,’ in which new ways of collaboration are required in order to break existing divisions of labour. One of the main goals of engagement and collaboration approaches is promoting reflexivity. I share the authors’ view of reflexivity as dialogue about long-term goals, imagined futures and implicit assumptions about the application of science and technology. An empirical study, ‘post-ELSI’ mode is found in Balmer & Bulpin (2013), who report a collaboration with an iGEM team<sup>50</sup> of the University of Sheffield in 2010. Following ‘Human Practices’ (Rabinow & Bennett, 2012), the authors aimed to ‘co-create’ a form of *equipment* that both resembled the engineering ethos of synthetic biology and helped to explore roles and relations of the team. Borrowing from the language of electrical engineering (which inspires synthetic biology), ‘sociotechnical circuits’ were developed; they consist of a visual representation of the roles and relations of the team as an electronic circuit, as the project underwent execution. Myskja and colleagues (2014) reply to the post-ELSI manifesto of Balmer and colleagues by claiming that “we have never been ELSI.” They see ELSI as a set of practices and guidelines, far from being a finished product that should be understood as undergoing transformations that are necessary (preserving its inherent interdisciplinary), instead of replacing ‘ELSI’ for a brand new ‘post-ELSI.’

An important feature of post-ELSI is the emphasis on collaboration with social scientists on the same hierarchical level. This may take the form of a convergence worker, to act as a mediator between science and society, a ‘boundary subject’ who attempts to connect the social with the science (Stegmaier, 2009). Calvert & Martin (2009) distinguish between a ‘contributor’ –“an easily plugged-in ELSI expert who enters the scene after the scientific knowledge has been produced”– (ibid., p. 204) and a ‘collaborator’ who takes an active role reflecting on and giving feedback about the processes scientists have underway. The role of the collaborator is still flexible and open to interpretation, as “scrutinizing the assumptions underlying the research of both natural and social scientists, and challenging habitual ways of thinking among both groups” (Calvert & Martin, 2009: 204). Rabinow & Bennett (2009) also made a distinction between ‘cooperation’ and ‘collaboration.’ They see cooperation as reminiscent of ELSI practices, where social scientists would fill out safety forms, and conduct

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<sup>50</sup> iGEM stands for the International Genetically Engineered Machine competition, a worldwide synthetic biology competition for undergraduate university students, organized by MIT. See <http://igem.org>; see footnote **Error! Bookmark not defined.**

discussions with natural scientists as long as these do not interfere with ongoing research; it consists of well demarcated lines of work. On the other hand, collaboration involves an interdependent division of labour on shared problems.

The emergence of nanotechnology paved the way for new possibilities in steering the direction of technological change, giving scholars the chance to participate in the ‘construction’ of an emerging technology. Unlike ELSI, social scientists would no longer have to be restricted to dealing with consequences. Instead, they could help shape them, and anticipating consequences. Moreover, with emerging technologies came new opportunities for STS scholars to become ‘instruments of governance’ themselves (Barben et al., 2008). In the account of Jane Calvert (2013a) on her collaborative work with the synthetic biology community, she sees the role of the social scientist as the ‘trickster,’ as “someone who asks critical questions, who provides an alternative perspective, and to some extent disturbs engrained ways of thinking” (ibid., p. 187).

An approach to engagement rooted in the literature of Anthropology was suggested by Paul Rabinow & Gaymon Bennett's in their 2012 book ‘Human Practices.’ Along with graduate student Anthony Stavrianakis, Rabinow and Bennett coordinated the fourth thrust of the ‘Synthetic Biology Engineering Research Center’ (SynBERC),<sup>51</sup> providing ‘Human Practices’ with a new venue for exploratory collaborative work. Human Practices is best understood as an ‘experiment in collaboration.’ The goal of Human Practices was to design a novel form of *equipment* to enable *flourishing* in synthetic biology research (Rabinow & Bennett, 2012). They describe flourishing as grounded in Greek philosophy, related to thriving and living the good life (Rabinow, 2009: 305). *Equipment*, inspired in the Greek term *paraskeuē* and developed further by Foucault, can be understood as a toolkit of concepts, a sort of ethical technology, to guide flourishing. Equipment “connects a set of *truth claims*, *affects*, and *ethical orientations* into a set of practices” (Rabinow & Bennett, 2012: 31).

Rabinow and colleagues claim that the collaboration they envisioned did not succeed in SynBERC because researchers were not willing to collaborate, only to cooperate. Their account explains that synthetic biologists were willing to talk about ethics, assist meetings, and overall showed willingness to cooperate, but they were not willing to alter their research practices as a result of engagement with ‘Human Practices’ (ibid.). Their involvement in SynBERC did not turn out as they expected, due to asymmetries in power relations, and the

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<sup>51</sup> SynBERC was a multi-university research centre established in 2006 with a grant from the National Science Foundation, to turn into reality the ethos of synthetic biology of ‘engineering biology’. Funding for SynBERC has ended and the project has turned into the ‘Engineering Biology Research Consortium’ (EBRC). See [www.synberc.org/policy-and-practices](http://www.synberc.org/policy-and-practices) [last accessed July 11, 2018].

lack of attention from other principal investigators who did not show interest in ethical engagement (Rabinow & Bennett, 2012).

### 2.5.2 Collaboration in the laboratory

Laboratory engagement studies have placed emphasis on introducing reflexivity in the laboratory and influencing research agendas of scientists and stakeholders. Sociotechnical integration (STIR) can be understood as a ‘policy instrument,’ with the goal of making innovation better (Fisher & Mahajan 2006). STIR is supported by a framework of ‘midstream modulation’, which proposes that technology development can be influenced ‘midstream’, that is, research and development activities and processes. This situates it between ‘upstream’ and ‘downstream’ activities, allowing enough flexibility for change while still relevant for intervention (Fisher et al. 2006; cf. Schuurbiers & Fisher 2009). This line of work is aligned with evolutionary frameworks of governance that embrace the possibility of steering the development of technologies, influencing knowledge production and socio-technical outcomes” (Fisher, 2007). Hence, the possibility of ‘modulating’ the dynamics of science opens up (Rip, 2006a). STIR incorporates elements of a laboratory ethnography mixed with ‘action research.’ Briefly put, social scientists become ‘embedded’ for twelve weeks in their laboratory counterparts to explore the social and ethical dimensions of research and innovation in real time. It rests upon the assumption that reflection on social and ethical issues can alter the decisions that scientists make. To guide such reflection, STIR dictates the use of a ‘decision protocol’, a template for conducting semi-structured interviews, drawing also from ethnomethodology (Fisher & Mahajan, 2010). The protocol is applied when a decision is required, so possible courses of action are identified and an outcome is reached (Fisher & Mahajan 2006).

As a ‘proof of concept,’ Erik Fisher was an ethnographer of the Thermal and Nanotechnology Laboratory (TNL) at the University of Colorado, Boulder, where he ‘collaborated’ with a doctoral graduate student (Fisher, 2007). Fisher’s intervention was not aimed at introducing social or ethical considerations, but instead to ‘render ongoing decision processes more visible to the researchers who performed them’ (ibid., p. 156). Application of the STIR’s decision protocol led to a student choosing an alternative catalyst, ‘ferro-fluid’, not only for being a better catalyst, but because it was more environmentally friendly and less hazardous for human health. Fisher’s ethnographic work at the University of Colorado has become STIR’s flagship. Ever since, STIR projects have taken place in at least twenty different laboratories around the world.<sup>52</sup> Examples include engagement about responsible

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<sup>52</sup> See <https://cns.asu.edu/research/stir> for further information on STIR. [Last visited 14 July 2018].



innovation and patient engagement in reproductive genetics laboratories (Conley, 2014), Calleja-Lopez' integration in nanotechnology laboratories (Gorman et al., 2013), industrial biotechnology (Stavrianakis, 2012), and corporate R&D (Flipse, van der Sanden, & Osseweijer, 2013). Schuurbiens' (2011) STIR project focused on exploring *first-order* and *second-order* reflective learning in his integration in two molecular biology laboratories, following van de Poel & Zwart (2010). The former can be understood as focusing on technical aspects and interests of the researcher, or 'reflection 'within' the system', while *second-order reflective learning* refers to 'reflecting 'on' the system,' considering broader social and ethical dimensions.

Sociotechnical integration is not exclusive of Fisher's STIR but of various communities of integration in which collaborative engagement of expert practices is an underlying theme, where expertise that involves learning for participants (collaborators) is valued (Fisher et al., 2015). These authors developed a framework to capture and analyse such diversity of approaches, represented in a two-dimensional matrix *values* (related to commitments and goals) on one axis and *capacities* (related to resources and additional knowledge) on the other. They suggest that STIR and Human Practices introduce 'alternative values.' Human Practices bring new societal and ethical dimensions into natural science research with its own parameters and constraints (i.e., flourishing), whereas STIR is different in the sense that it seeks to clarify and broaden existing concerns, so they arise 'from within.' The framework is useful to explain why Human Practices did not succeed. It bears an additional stress upon natural scientists, as they would have to learn (and unlearn) new values in addition to their own existing commitments (Fisher et al., 2015).

Additional forms of engagement with scientists include Robert Doubleday (2007b) postdoctoral researcher as an ethnographer with the Nanoscience Centre of Cambridge University, where his role became more of an 'enabler of interactions' essential for public engagement activities (such as NanoJury UK), that sought to shape nanotechnology as a public object, and a representative of public opinion for the nanoscientists (Doubleday, 2007b, 2007c). In the process, his involvement allowed for scientists to detach from the process, or disengage, leaving the bulk of public relations to the embedded social scientist (Doubleday & Viseu, 2010). Furthermore, social scientist Ana Viseu faced a similar situation to Doubleday, while hired by the Cornell NanoScale Facility. In her 'integration' she was allocated workload that was not related to her goals as an ethnographer, such as conducting outreach activities like designing a webpage and developing a video on the social and ethical implications of nanotechnology (ibid.).

From a perspective less inspired by policy mandates, ethicists and philosophers have also attempted to inquire about social and ethical issues to the laboratory. McGregor & Wetmore

(2009) conducted an ethnography in a bio-optics laboratory, in which they found the laboratory to be very efficient for engaging students and researchers on ethical issues, better than lecturing about ethics. Likewise, Tuma (2013) addressed ethical and social questions as the ‘in-house’ ethicist of an R&D nanotechnology facility in the United States, where clients could hire state-of-the-art equipment to perform experiments. A hallmark in prompting dialogue with scientists is Rosalyn Berne’s (2006) *Nanotalk*, a book about her interviews with nanoscientists about ‘deep’ questions, such as “what it means to be human in a nanotechnology-driven world?” (Berne, 2006: 58).

Workshops have been an important avenue for social research, for instance constituting a fundamental component of ‘constructive technology assessment’ (CTA) (cf. Schot & Rip, 1997; te Kulve & Rip, 2011; Rip & Robinson, 2013; Robinson, 2009). Frow & Calvert (2013) conducted an illustrative study of how social scientists can foster discussion about future possibilities for synthetic biology. The authors held two workshops in major synthetic biology conferences (SB 4.0 Conference 2008 and 2009 BioSysBio meeting in Cambridge, UK) with synthetic biologists and other actors (policy/NGO representatives). The format of the workshops was informal and flexible. Through one-sentence scenarios, the authors aimed to foster how thinking about the future influenced present-day practices, prompting thought about the sort of choices to be made in the present. Similarly, the ‘walkshop’ approach (Wickson, Strand, & Kjølberg, 2015) takes the workshop outside of the meeting room to hold discussions with natural scientists during walks outdoors as they move along scenic landscapes in the Norwegian countryside. Walking in this sense ‘facilitates embodied dimensions of thinking’ and facilitated engagement between participants as ‘multidimensional individuals’ (ibid., p. 262).

As collaboration between social scientists belong to a wider concern over interdisciplinarity, other advances in the field have paid more attention to philosophical dimensions. The ‘toolbox (of philosophical dialogue) project’ (Eigenbrode et al., 2007) falls in this category. It assumes that obstacles for collaborations between different originate in different epistemological and metaphysical assumptions. Thus, the project seeks to improve interdisciplinary collaborations by fostering discussion among collaborators about the philosophical assumptions that guide their work.<sup>53</sup>

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<sup>53</sup> There is a vast body of literature on interdisciplinarity, philosophy and values; see for example Wallington & Moore, 2005.

## 2.6 Summary

In this chapter I have gathered elements for the analysis of the data I collected in my fieldwork and secondary sources that I present in Chapters four to seven. As this is one of the first systematic studies of social aspects of xenobiology, it is important to situate it in comparison to social studies of synthetic biology, the parent branch of xenobiology. From synthetic biology I gather the disposition to collaborate with researchers in the life sciences and the tools to study the 'ethos' and meanings that are formed in a collective manner (as a community).

The studies in the literature I present afterwards feed into three categories of analysis that I argue. First, concepts like co-production, imaginaries, and areas like the sociology of expectations and public understanding of science, provide theoretical tools to analyze the promises and narratives of xenobiology that are oriented toward the future. As I place emphasize on the work in xenobiology that narratives, visions and imaginaries perform, as reflecting dynamics of scientists and society, this set of theoretical works prove useful.

Second, for examining the relationship between biocontainment and xenobiology, and the framing of such a necessity, it is useful to refer to studies that have conceptualized the role of safety and technological design in new technologies. Safety, one among many values, says much about what societies care about in new technologies. The literature in this stream, along with sociology of risk, is useful to open up avenues for thinking about managing the unknowable downsides that xenobiology may bring; in this sense, works on collective and real-world experimentation are relevant, because matters of risk and safety are also questions of power and authority.

Last, I present literature about ethics and collaboration between social scientists and life scientists, that guided my efforts to introduce questions to xenobiologists about the wider ramifications of their work. The literature on governance of technology has made excellent progress in conceptualizing responsibility, public participation, and decision-making about technoscience and scientific controversies. I place emphasize on the practical challenges of social scientists of entering the laboratory and helping to steer the trajectory of new technologies, with a focus on addressing the motivations and institutional arrangements that make difficult interventions.

In the next chapter I describe the methods and the rationale for collecting the data that constituted the bulk of the analysis presented in this thesis.

## 3. Methodology

### 3.1 Introduction

In this thesis I explore how the development of the emerging discipline of xenobiology challenges our understanding of life and reflects the current approach to the governance of the relationship between science and society by narrowing matters of concern to risk and safety that can be addressed via design principles. The methods adopted in this research attempt to capture the role of sociotechnical imaginaries (see previous chapter) and imagination in guiding the efforts and practices of xenobiologists. This thesis reports on an emerging technoscience (xenobiology) using a combination of data collection methods. The bulk of my data comes from a series of thirty-four semi-structured interviews conducted over one year. This was complemented with participant observation in a synthetic biology laboratory for one year, where I also led discussions with researchers about crucial topics of science and society related to xenobiology. In addition, I analysed policy and scientific literature about advances in xenobiology, biosafety and biocontainment. I complemented these approaches attending academic events (i.e., conferences, workshops, seminars) about synthetic biology and xenobiology.

The research presented in this thesis subscribes to a qualitative research tradition that aims to create understanding from data as the analysis proceeds. This differs from studies that start with an understanding to be tested, where often the hypothesis dictates the form, quantity, and scope of required data. Research design is moulded by the method (rather than dictated), and is responsive to the context of participants (Richards & Morse, 2007). Qualitative researchers acknowledge that views of the world are based on values and dispositions, and instead of looking for laws, their aim is to achieve a sense of meaning and deep understanding of the subject under study (Smith, 1983). Nevertheless, if qualitative research produces knowledge that is context-bound, it does not deny the possibility of understanding many contexts or developing abstractions that may apply across contexts (Bradley, 1993). In qualitative research the researcher does not seek 'universal' generalizations from a case study, but rather 'understanding' of phenomena or trends in more depth that can be reached with quantitative research; it places emphasis on how individuals construct and make sense of their world (Robson, 2011). The most important is qualitative research's exploratory approach, which allows to focus in depth at the narrative structures through which scientists perform their role as scientists and engage with the materials and spaces of everyday life. Qualitative research attempts to understand the worldviews of the subjects being studied, how the subjects think about the world, and what their motivations, anxieties, and agency

are as humans.

Qualitative research is useful for the goals of STS, a discipline that looks at how technological objects and practices are constructed. Biotechnological developments present far-reaching political, economic, and ethical ramifications that raise questions a number of questions: such as the goals, uses and ownership of research, the relationship of humans to the world, shifting definitions of nature, along with distribution of risks, benefits and access to new biotechnologies. Such challenges should be addressed with scientists because they have the power to change technological trajectories or reify them.

The data I present in this thesis mainly comes from two methods, participant observation and semi-structured interviews with participants. I also participated in academic events, organized discussions with life scientists, and studied secondary sources (published and video materials). These approaches complement each other. In the case of participant observation, it enhances the interpretation of data and provides information that individuals would not respond when interviewed (De Walt & De Walt, 2011). It is particularly useful to explore new themes or generate hypothesis, “enabling researchers to know what questions to ask,” and lessening reporting bias (Guest et al., 2013: 80-81). Hammersley & Atkinson (2007: 3) explain, “Ethnography usually involves the researcher participating, overtly or covertly, in people’s daily lives for an extended period of time, watching what happens, listening to what is said, and/or asking questions through informal and formal interviews, collecting documents and artefacts.” Importantly, in participant observation the analyst studies participants in their everyday context, providing a wider range of data that complements what can be found in an interview setting. Observation is separate from conversations, it adds further layers of meaning to personal interactions (Becker & Geer, 1957). Studying scientists in their workplace helps to set distance from the meanings they convey through interviews, since talk is not always related to action; people do not always say what they mean (Jerolmack & Khan, 2014).

Interviews are classified into three broad categories: structured interviews, semi-structured interviews, and unstructured interviews (Fielding, 2006). The former aims at the standardization of responses that make data comparable and aim to avoid the influence of the interviewer in the responses of participants. On the other hand, unstructured interviews are more of an open conversation, more exploratory. Interviewing participants is for Saldaña (2011: 32) an “effective way of soliciting and documenting, in their own words, an individual’s or group’s perspectives, feelings, opinions, values, attitudes, and beliefs about their personal experiences and social world.” Interviews are limited to self-reported data by participants, depending on how much information they want to share, and how they understand such information (or perspectives); such understanding is related to how

experience influences what individuals think and how they think about it (Kvale, 2008). Through conversations (i.e., interviews) the researcher initiates an exchange of ideas and perspectives which the interviewee may not have thought about. In this sense, the analyst plays an active role as a facilitator of reflection, to dig up meanings from participants and helping them articulate a point of view on particular topics. This does not mean that the researcher looks for ideas that are not existent, but all the opposite, plays a role in extracting and forming the ideas of participants. The researcher should aim for learning from his participants, trying to understand the world through their eyes.

In my fieldwork I focused on the worldviews of researchers involved in synthetic biology and xenobiology. In contrast with other studies about public perceptions of new biotechnologies (i.e., Gaskell, 2004; Gaskell & Bauer, 2007; Marris et al., 2001), xenobiology is in such an early stage that it has not captured the public's imagination and its realization is far from products or objects that publics can relate to. At an early stage of my data collection I aimed to gather perspectives from both researchers and other actors like decision makers, civil servants, and civil society members. I conducted interviews with three civil servants from a British science funding agency, two civil society members, and two biosecurity and biosafety experts (more below). I decided to not continue further down this path and instead focus on researchers for two reasons. First, the actors I interviewed were not familiar with the state of the art of xenobiology, so our conversation centred around issues in synthetic biology; I did not anticipate this since I selected these participants because of their roles in their organizations, rather than their involvement with xenobiology. I am not aware of civil society organizations that have engaged directly with xenobiology. Second, I made the effort to reach out to members of relevant organizations that support or fund xenobiology-related approaches, such as ERASynBio,<sup>54</sup> the U.S. National Science Foundation, or the European Commission, without success.

As a field in the making, it is likely that my participation in xenobiology will influence to some degree the development of the field (Calvert, 2013a). Besides participating in academic events and having conversations with researchers, my interactions were oriented toward engaging and trying to raise reflexivity with the makers of the field. My study of the field may give visibility to the field, which I argue spokespersons of xenobiology seek: visibility and attention in a knowledge production regime where these two properties are scarce and vital for attracting resources and reputation. However, in this thesis I give priority to questions about responsibility and control; if my work influences the field it will likely be for

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<sup>54</sup> According to the website [www.erasynbio.eu/](http://www.erasynbio.eu/) [last visited August 11, 2017], "ERASynBio is an initiative of international funding agencies working together to promote the robust development of Synthetic Biology and to structure and coordinate national efforts and funding programs. The network was created in 2012 and funded as an ERA-Net by the European Commission under FP7 until 2014."

not taking the promises of xenobiology at face value, but to question their origin, their motivation, and challenge how they embed forms of power in biotechnological objects.

Because the researcher is the instrument in qualitative inquiry, a qualitative report must include information about the researcher. The presence of a fieldworker can certainly make a difference in the setting under study: it may create tension and anxiety that alter performance of the social group. The researcher can affect the setting through its own actions, for example conversations can be a source of new ideas and reflection for the social group (Patton, 1999). My data collection and analysis may have been influenced by my former education in the life sciences. Through my undergraduate degree in Microbiology and subsequent Master's degree in Biochemistry some time ago I learned the basics of molecular biology tools and gained experience in laboratory techniques and familiarity with a molecular biology laboratory. Such background has facilitated me the understanding of the literature in xenobiology and having conversations with xenobiologists about the science involved. I am aware that such sensitivity to xenobiology could have inclined me to see certain routines or practices of researchers as 'normal.' I made the effort to be reflexive about my role in the development of xenobiology and how my previous background and experiences may have inclined me to observe and interpret my fieldwork in particular ways. In the laboratory and when interacting with research participants, as well as analysing data and writing about it, I aimed to maintain a rigorous and analytical mindset.

### **3.1.1 Studying the laboratory**

The site for my participant observation was a synthetic biology laboratory located in a university in London. This choice of site requires clarification, since the laboratory is not necessarily the best place to study the relationship between scientists and society. Thomas Gieryn (1995) argued that explanations for the cultural authority of science need more analysis than the descriptions of what goes on at the laboratory bench; he claims that STS needs 'getting constructivism out of the laboratory' and moving 'closer to places where matters of power, control and authority are settled' (*ibid.*, p. 440). The laboratory has been conceptualized as a place with a defined space, where scientific objects are "symbolically or politically construed, for example, through literary techniques of persuasion such as one finds embodied in scientific papers, through the political stratagems of scientists in forming alliances and mobilizing resources, or through the selections and decision translations which "build" scientific findings from within" (Knorr-Cetina, 1992: 115). Hierarchies and tasks are established in the laboratory, where the day-to-day activities of scientists occur.

The foundations of STS contain studies of what occurs in the laboratory in order to demystify an internal privilege of science to achieve truth. Two main different approximations to ethnography have been attempted in STS. In *Laboratory Life* (1978), Latour and Woolgar entered the laboratory as a stranger looking at a tribe, detached from the scientific knowledge that guides the actions of scientists; this is necessary to analyse the social world of scientists without being influenced or biased by their epistemological commitments. On the other end of the spectrum is Harry Collins' approach, for whom the best sociological analysis is the result of forming tight connections with scientists and learning their trade and theory, because he considers that understanding the scientific discipline that an ethnographer studies is necessary for properly understanding their social world (cf. Collins, 1983). However, getting too involved with informants and familiar with their research can risk becoming 'naturalized,' losing the capacity to be surprised or notice important patterns that should inform the qualitative analysis. Differing approximations owe to disciplinary foundations like placing emphasis on the role of culture (in the case of anthropology) or sociological theories (Hess, 1998).

Nevertheless, this still leaves unaddressed the question of why the laboratory can be a good place for studying visions, imaginaries and narratives of xenobiology. It is where the materiality and expectations about technology coalesce, and scientists ascribe meanings to novel biotechnological objects. It is where the uncertainty of what is biologically possible and acceptable for society meets the pressure of gaining resources to keep the lights of the laboratory on. Importantly, it allows the analysis of the "conceptual and material building blocks of expectations" (Lucivero, Swierstra, & Boenink, 2011: 134). As such, it is also a place of cultural production, a prime site where potential futures are tested via experiments and ways of thinking about life. It is in the laboratory where expectations can be reframed, and sociotechnical imaginaries can be made visible to scientists (Gjeffsen & Fisher, 2014).

In my fieldwork I did not emphasise semiotic analysis, but rather the content of conversations with scientists to look for constructs (like safety or limits) that participants articulate from their own perspectives and language. In contrast with laboratory ethnographies that have focused attention on knowledge production or science "in the making" (Latour, 1987), the participant observation presented in thesis focused on discourses and meanings that researchers attached to experiments and knowledge production in xenobiology, and to a lesser extent, the materiality of research in xenobiology –what it is like to conduct experiments in the field, and how they may shape how researchers think about the ramifications of such experiments.



## 3.2 Data collection methods

### 3.2.1 Semi-structured interviews

Conducting interviews is a widely used method in qualitative research. I selected candidates for interviewing based on their contribution to scientific articles on xenobiology, after a literature review on the topic and frequent search for new articles in scholarly databases like Web of Science™. I also found potential interviewees by tracking citations in articles about xenobiology or biocontainment and asking other interviewees or members of the laboratory where I conducted participant observation, following a ‘snowball approach.’ The list of participants in the xenobiology conferences in 2014 and 2016<sup>55</sup> was also useful to identify potential candidates. It is important to note, the community of researchers conducting research that can be classified as xenobiology is small with no more than fifty researchers that have tangential relationship to the field. This made the process of identifying potential interviewees easier. Also of importance, I abstained from interviewing two major proponents of xenobiology, Markus Schmidt and Philippe Marlière, since I thought this would create a type of binding relationship that would reduce my flexibility to interpret and discuss their public speeches or articles. Nevertheless, I had the opportunity to meet these representatives of the field in person (at academic events) and these interactions helped shape the analysis presented in this thesis.

Interviews took place in the offices of researchers or in cafés (in the case of students or visitors from another cities), and some were conducted over using Skype when interviewees that were not physically present in London. Each interview was tailored towards the profile of the interviewee, considering factors such as the degree of expertise in xenobiology and contributions to the field; for each semi-structured interview I used an ‘interview guide.’ Interviews lasted between half an hour and one hour, depending on the availability of the interviewees. Conversations were recorded using a mobile phone and a digital audio recorder, in case either artefact failed to record; I stored the digital audio files in my computer. For transcription I used the freely available software InqScribe® that provided useful features like slowing down the pace of the voice or skipping back seconds to amend the transcription. At all times I maintained the anonymity of participants in this study, by using labels to refer to them (i.e., 1A, 12C), given that full anonymity cannot be achieved. **Table 1** provides a list of the interviews conducted, along with demographic information about gender and location of workplace.

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<sup>55</sup> See footnote 14.

<b>Label</b>	<b>Category</b>	<b>Work based</b>	<b>Gender</b>	<b>Position at time of interview</b>
01A	Environmental & technology governance NGO	Canada	Male	NGO member
11A	Xenobiology/Synthetic biology	United Kingdom	Male	Postdoctoral researcher
12A	Synthetic biology	United Kingdom	Male	Reader
12B	Synthetic biology	Denmark	Male	Postdoctoral researcher
13A	Xenobiology/Synthetic biology	Belgium	Female	Postdoctoral researcher
13B	Xenobiology/Synthetic biology	United States	Female	Doctoral student
14A	Xenobiology/Synthetic biology	United States	Male	Doctoral student
16A	Synthetic biology	United Kingdom	Male	Associate Professor
16B	Synthetic biology	Spain	Male	Group Leader
17A	Xenobiology/Synthetic biology	Germany	Male	Group Leader
18A	Synthetic biology	United Kingdom	Female	Postdoctoral researcher
19A	Synthetic biology	United Kingdom	Male	Professor
22A	Government agency	United Kingdom	Female	Civil, servant
22B	Government agency	United Kingdom	Female	Civil servant
23A	Government agency	Belgium	Female	Senior scientist
25A	Environmental & technology governance NGO	United Kingdom	Female	NGO member
26A	Xenobiology/Synthetic biology	Belgium	Male	Professor
27A	Synthetic biology	United Kingdom	Male	Reader
28A	Synthetic biology	United Kingdom	Male	Doctoral student
28B	Synthetic biology	United Kingdom	Male	Doctoral student
28C	DNA nanotechnology	United Kingdom	Male	Doctoral student
28D	DNA nanotechnology	United Kingdom	Male	Doctoral student
29A	Genetic engineering of mosquitoes	United Kingdom	Male	Professor

2A	Xenobiology/Synthetic biology	United Kingdom	Male	Reader
5A	Synthetic biology	United Kingdom	Male	Associate Professor
5B	Synthetic biology	United Kingdom	Male	Former Postdoctoral researcher (retired from research activities)
5C	Xenobiology/Synthetic biology	United States	Male	Professor
5D	Xenobiology/Synthetic biology	Germany	Male	Professor
6A	Biosafety/biosecurity expert	United Kingdom	Male	Senior Research Fellow
6B	Xenobiology/Synthetic biology	United States	Male	Assistant Professor
7A	Biosafety/biosecurity expert	United Kingdom	Male	Director at consultancy firm
8A	Science policy expert	Germany	Female	Manager at research organization
8B	Xenobiology/Synthetic biology	United States	Male	Postdoctoral researcher
9A	Xenobiology/Synthetic biology	United States	Male	Postdoctoral researcher

*Table 1. Demographic interviews about interviewees in this dissertation. The numbering of 'labels' is based on the date of the month when the interview was conducted. This numbering is used to preserve the anonymity of the interviewees.*

### 3.2.2 Participant observation in a synthetic biology laboratory

Obtaining permission from the principal investigator to study his laboratory as participant observant was the result of establishing trust and interest since the early stages of this project. I initially approached the principal investigator with an interest to learn about xenobiology. After checking relevant literature in xenobiology, I met with the principal investigator to ask for his permission to study his laboratory; he showed interest and agreed to allow me to study his laboratory. However, he explained that he would have to discuss the possibility with his group. He was concerned that my study could harm the reputation or career progression of his group, so he requested to have access to any writing output I would produce. Subsequently, the principal investigator informed me that his group had accepted my participation in the laboratory. I met the members of the laboratory for the first time in an informal setting, a pub, which provided a relaxed atmosphere to introduce myself. During this meeting in the autumn of 2015, the principal investigator asked me to introduce what I would be doing in my fieldwork. I agreed with the principal investigator that I could participate in the group's weekly meetings as an invited guest, without taking notes until I gathered the ethical approval from my department. The group consisted of twelve members,

including Master's and doctoral students, technicians, post-doctoral researchers, and undergraduate students (with whom I had less interaction).

Participant observation in the form of weekly group meetings constituted the bulk of my data collection because they were a space for discussion. They took place in a room inside the building where the laboratory was located. Each meeting began with a brief discussion on administrative and 'housekeeping' issues, like ordering reagents. Then there were two slots of half an hour for one member of the group, in which they presented either the summary of a research article or an overview of their latest work in the form of 'work in progress.' Both types of talks provided sufficient material for the group to discuss possible scientific solutions to roadblocks, clarify questions between members and exchange opinions about the state of the art in xenobiology and synthetic biology.

Once I obtained ethical approval from my department, I met individually with each member of the laboratory to discuss the informed consent I had sent in advance and clarify any questions they might have had. After two months of individual meetings, all members of the laboratory accepted to be part of the study. During our conversations, some researchers were concerned about maintaining the confidentiality of their research. Some worried that I could share the results of their research with other laboratories or give away plans for patent applications. The main challenge I faced was to earn their support for my study and gain their trust. It proved difficult to observe researchers conducting experiments because they would usually say there was nothing interesting to see (so there would be no need for me to join them), they needed to focus on the technique so they could not talk to me, or were too busy. Beyond the reasons they provided was the absence of an incentive for integrating me into their workplace. Nevertheless, two researchers at different stages of their career (doctoral studies and post-doctoral research) welcomed me to their experiments. They showed me a variety of experiments they conducted and were very open in explaining their work and engaging with my questions.

Following a classical piece of advice for conducting ethnography, I volunteered to carry out work in the laboratory as a strategy to be valued by the group,<sup>56</sup> and gain access to material practices through which participants engage with their local context. I made the case that my background in microbiology and biochemistry could be useful. This request was not immediately welcomed by the members of the laboratory nor the principal investigator; they explained to me that although my help was welcome, it would require from them more work to rearrange tasks and training me, so they declined my offer. However, after half a year, the principal investigator invited me to assist a doctoral student in carrying out gene

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<sup>56</sup> Helping with tasks in the laboratory is a common device that has been used by other analysts of laboratories, cf. Finlay, 2013; Latour & Woolgar, 1979.

cloning procedures, which did not require much expertise. This provided a valuable opportunity to perform experiments (or activities) and gain another perspective of the materiality of synthetic biology. The tasks I performed could be considered ‘mundane,’ as they were well standardized in molecular biology and involved the use of commercially available kits, for example for extracting DNA from bacterial cells, or inserting segments of DNA into new plasmids. The project I helped with provided to me an opportunity to be in the laboratory not only as an observer, but as an experimenter. The laboratory plan was similar to common molecular biology laboratories, with a central hallway and one row of benches on each side of the hallway. Outside of the laboratory and down a corridor there was an entrance to the office space of the laboratory. The office had an open plan where each researcher had a computer located in a long desk that provided space for rows of four researchers. I was lucky to have been allocated a small desk since the beginning, which would provide a spot for me to stay close to the laboratory and carry out tasks for this thesis (i.e. reading articles).

My role in the laboratory involved watching the preparation and execution of experiments, sitting in weekly group meetings, as well as joining social activities such as evening drinks and celebrations of birthdays (i.e., gathering to eat cake). I took field notes during meetings and activities, without immediate interpretation, “as seen and heard by the researcher” (Maykut & Morehouse 1994: 67-68), taking into account that “a good ethnography is only as good as the field notes upon which it is based” (Shaffir, 2004: 385). I also attended departmental talks and conferences on synthetic biology. I engaged with the members of the laboratory throughout these activities, where I could ask for more detail or explanations about the observations I made. In order to conduct open-ended interviews with members of the laboratory that I could record, I asked them to meet individually for half an hour to talk about their perspectives on science and society; I conducted these interviews between one and three times with participants. In these interviews I asked them about events in the laboratory and their perspectives on different topics of politics, ethics and social issues in xenobiology.

Conducting participant observation did not come without challenges. In my fieldwork I found it difficult to fit in or build rapport with the group; ‘hanging out’ did not come easy. I did maintain good relationships with the laboratory although researchers were not always were approachable and willing to have me accompanying them in their activities. Language barriers also came into play. As English is not my first language, it is slightly difficult to make jokes or speak fluently with members of the laboratory, which would have made forging strong relationships easier; this was particularly the case when I was in social environments

like a pub, where I had difficulties listening to what others said and making myself understood.

### 3.2.3 Attendance of academic events

I complemented data collection with participation in academic events that were related to synthetic biology and xenobiology. These included conferences, departmental talks, workshops, and symposia that took place in London, Edinburgh, Berlin and Cambridge (US). Conferences are important sites for studying the production and circulation of knowledge as well as establishing of academic identities and hierarchies (González-Santos & Dimond, 2015). They also serve to build trust and a sense of community between researchers (Collins, 2004; Dimond, Bartlett, & Lewis, 2015).

Attending academic events allowed me to observe and interact with scientists in rich atmosphere in which I had opportunities to observe discussions between researchers (and the types of questions they ask and give importance to) and have the opportunity to raise different conversations with scientists, such as commenting on the content of a talk during a break. Attending gave me access to a set of researchers different from interviewees and members of the laboratory that were important for shaping my thinking behind xenobiology. These events were also valuable for noticing social circles that researchers constitute, in terms of who is a friend of whom, who tends to stick with whom, and what types of researchers tend to hang out together (i.e., graduate students with graduate students, American researchers with American researchers, and so on).

I highlight my attendance at the second xenobiology conference (XB2) held in Berlin in 2016 from May 24 to 26,<sup>57</sup> organized by Phillipe Marlière and his biotech company Isthmus SARL,<sup>58</sup> held in the Berlin Brandenburg Academy of Science. The conference was organized with funds from European Union grants, according to the organizers.<sup>59</sup> Similar to the first xenobiology conference, in the second (academic) conference “*Synthetic scientists and industrialists will reconvene on 24-26 May 2016 in the historical center of Berlin to share their views and visions on recent and future advances in Xenobiology.*”<sup>60</sup> (Emphasis original). The content of the program was oriented toward recent advances or theoretical insights in xenobiology. Of

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<sup>57</sup> See the second xenobiology conference website at <http://xb2berlin.isthmus.fr> [last visited 12 August 2018].

<sup>58</sup> See <http://www.isthmus.fr> [last visited 12 August 2018]

<sup>59</sup> Another academic event that deserves mention in detail is ‘Xenobiology: Biosecurity, Biosafety and Biocontainment’, that took place in Birkbeck College on July 5th, 2017. This event also offered spaces for researchers to present their latest work, but also the opportunity for researchers to discuss key themes in xenobiology in panels.

<sup>60</sup> See footnote 57.

importance, in the conference there was a panel session titled ‘The Future of Life is Synthetic: The Promises of Xenobiology’ (**Figure 3**) that took place in the late afternoon and was open to the public. Participants in the panel included xenobiologists Philippe Marlière and Phil Holliger, risk assessment expert Markus Schmidt (from Biofaction), philosopher and ethicist Heiner Fangerou (Heinrich Heine University), and molecular biologist Bernd Müller-Röber (University of Potsdam). This provided a valuable scenario for observing input from a non-scientific audience about xenobiology.

The poster is a vertical layout with a red header and footer. The header contains the text 'PANEL DISCUSSION' in white on a red background, with a circular logo of the Berlin-Brandenburg Academy of Sciences and Humanities (BBAW) partially visible. The top right corner features the BBAW logo and name. The main title is in large, bold, red letters. Below the title is a paragraph of text describing the session's funding and organization. The date and time are in red. The location is in black. There are three columns of text: a main body of text, an 'Introduction' section with a photo of a mammoth, and a 'Panel Discussion' section listing participants. Logos for SOF, ITHMUS, Schering Stiftung, and Leibniz Vision als Aufgabe are at the bottom. The footer contains contact information.

**PANEL DISCUSSION**

berlin-brandenburgische  
AKADEMIE DER WISSENSCHAFTEN

**THE FUTURE OF LIFE IS SYNTHETIC:  
THE PROMISES OF XENOBIOLGY**

A Science & Society Session funded by the Schering Foundation, jointly organized by the projects "Gene Technology Report" and the Annual Theme 2015|16 "Leibniz: The Task of Visions" of the Berlin-Brandenburg Academy of Sciences and Humanities, and the Second Conference on Xenobiology

**Wednesday, 25 May 2016 / 6 pm**  
Berlin-Brandenburg Academy of Sciences and Humanities  
Leibniz Hall, Markgrafstraße 38, 10117 Berlin

Tremendous technical advances have been made in the life sciences in recent years. Scientists are now able to alter and analyze genes with an ease never seen before. Whole genomes can be built from scratch and transplanted into living cells. But has this brought us any closer to understanding life?

Synthetic biology in particular has been heralded as an exciting new field which will allow a deeper knowledge on how living systems "work". Synthetic biologists extensively manipulate organisms at DNA level. Even bringing long lost species such as the woolly mammoth back to life from recovered DNA samples seems possible nowadays. Xenobiologists reach further yet – aiming to create artificial life built out of synthetic chemicals instead of natural DNA.

Such new biologies promise groundbreaking solutions for pressing global problems. However, these possibilities have raised concern about their future environmental and societal impact, and how they might change the way we think about life, biodiversity and evolution. Our interdisciplinary panel will bring together renowned experts from xenobiology and the philosophy of the life sciences to explore these and other matters of humanly-created life.

*Admission is free. Registration is required.*

**Introduction**  
**Bernd Müller-Röber**  
University of Potsdam  
Member of the BBAW

**Panel Discussion**  
**Philippe Marlière**  
Scientist of Fortune S.a., Luxembourg

**Philipp Holliger**  
MRC Laboratory of Molecular Biology,  
Cambridge UK

**Heiner Fangerou**  
Heinrich Heine University, Düsseldorf

**Markus Schmidt**  
Biofaction, Vienna, Austria

**Moderated by**  
**Kai Kupferschmid**  
Science Journalist

Picture: fotolia.com / auntspray

**SOF SCIENTIST OF FORTUNE** **ITHMUS** **SCHERING STIFTUNG** **LEIBNIZ VISION ALS AUFGABE**

**Further information:**  
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www.bbaw.de

Figure 3. Poster for panel discussion open to the public about the promises of xenobiology, in the second xenobiology conference (2016).

### 3.2.4 Secondary sources

In this thesis I have used additional secondary sources, that I divide in two categories. The first category includes texts, such as review articles, scientific articles, policy reports, and reports from learned societies. Review papers, and the introduction or discussion of scientific articles, are useful because they present claims about the present and future of xenobiology. In summarizing the state of the art, authors of review articles assess what they see as important steps that have been taken and highlight the next steps. Secondly, I employed publicly available sources that included interviews with scientists in newspapers and radio, videos of conference talks (usually available in YouTube or Vimeo), documentaries and videoclips about synthetic biology, and formal interviews to synthetic biologists (like the SynBioSAFE project).<sup>61</sup> Altogether, these sources complement the interviews and participant observation I conducted, because they provided access to the perspectives of actors in different contexts; interviews are not neutral and the setting in which they take place influence how open the interviewee will be when expressing opinions or favouring particular views of a subject.

The search for secondary sources was conducted during the whole duration of this project, there was not a phase dedicated to identifying and analysing secondary sources. I searched for secondary sources in a web browser (Google) and the video-sharing platform *YouTube*; I did not consider necessary a systematic and comprehensive coverage of news and media, because the material I sought was meant to support the empirical data I planned to gather. I used a variety of search terms, including the names of scientists in the field (i.e. George Church) whom I knew from the scientific literature and their participation in synthetic biology conferences, this suggested that they conducted research in synthetic biology and xenobiology. In looking for interviews or press coverage of scientists, I also searched for their laboratories' websites, which usually include an overview of their research goals and disciplinary standing. Search terms included 'XNA,' 'xenobiology,' 'synthetic biology,' 'biocontainment,' 'genetic code engineering,' 'genome engineering,' along with words like 'interview,' 'public,' 'panel,' 'conference,' and 'lecture.' The type of secondary sources based on media representations are valuable in two aspects. First, how they portrayed (or cited) scientists and actors, who often would provide their opinion on synthetic biology or the article they recently published. Second, secondary sources are also available to trace how

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<sup>61</sup> SynBioSAFE was a scientific project supported fully by the European Commissions's FP6 programme. It was the first project in Europe to research the safety and ethical aspects of synthetic biology – see <http://synbiosafe.eu/96-2/> (last visited September 29, 2018). The project's website contained short interviews (up to five minutes long) with renowned scientists and stakeholders in synthetic biology. I transcribed most of these interviews that were available on the website; at the time of writing, these interviews were no longer available.



public opinion receives discoveries in the life sciences. Even though this analysis was not oriented toward a systematic analysis of media representations of scientific news, the framing of texts and interviews provides clues that add to the overall analysis of the data I collected.

Noteworthy, advances in synthetic biology and xenobiology have received abundant media coverage, perhaps due to pushing the frontiers of knowledge in biology. Scientific journal publications about xenobiology have attracted the attention of journalists. For instance, the publications of the laboratories of Farren Isaacs (Rovner et al., 2015) and George Church (Mandell et al., 2015) in January 2015 attracted wide media coverage, because they reported the requirement of engineered *E. coli* to survive with the supply of artificial amino acids, thanks to a 'recoding' of their genetic code; this requirement provides a form of biocontainment, which is the 'selling point' of these works. Another development was achieved by Floyd Romesberg in 2014 (Malyshev et al., 2014), whose research group engineered bacterium capable of copying DNA that contains unnatural nucleotides, as I illustrate in **Appendix one**, in which I provide an overview of scientific discoveries and advances in xenobiology; these works are not the first developments in xenobiology, but represent important achievements in terms of manipulating life, the politics and ramifications of which constitute an overarching theme in this dissertation.

By media coverage I mean interviews with authors of the articles, as well as news articles that incorporate quotes from authors and researchers in synthetic biology. I have indicated throughout this dissertation when I have used data from publicly available media sources. **Appendix two** displays a list of scientific articles that have received media coverage, along with a sample of news and media products, including interviews and panel discussions. This is expected to provide an overview of the breadth and variety of sources about xenobiology that the media has produced in recent years.

### **3.3 Bringing questions (or society) to the laboratory**

My participation in the laboratory was originally conceived as a form of engagement and collaboration with life scientists; myself being a social scientist– (cf. Calvert, 2013; Fisher & Schuurbiens, 2013; Rabinow & Bennett, 2012). The goal of my participation was to increase reflexivity in the laboratory, influencing its output in xenobiology. I originally planned to become an active member of the laboratory to co-construct novel narratives and visions about xenobiology, advice strategies for reaching the public and make the laboratory's research more open to critique and feedback. Throughout conversations and interviews I conducted with members of the laboratory I asked them about their responsibility as scientists, how they perceived the role of the public in their research, or what would be the

value of their research for society. I thought it would be valuable to create a space in the laboratory to formally introduce these questions to the group in the form of a group discussion (similar to a focus group), so I asked the principal investigator to allocate myself time in the weekly meetings where I could lead a discussion on topics of my choice. Over the course of a year, I was allocated five slots for leading a discussion with the group. I used such slots to host what could be best described as focus groups, a guided discussion between members of the laboratory. Focus groups are a useful way to elicit opinions in a group (Lezaun, 2007). They create artificial interactions between participants about topics that otherwise they would not be discussed at the intensity and depth required. Moreover, individuals may provoke discussions in ways that the researcher would not anticipate or could not recreate himself (Morgan, 1997).

I saw leading discussions with the laboratory as an opportunity to bring society *back into the laboratory* and provide elements that could motivate researchers for further reflection on their role as scientists in society. I did not expect to see a change in the course of the experiments or the agenda of the laboratory during my fieldwork, but over the long run my role could have left a legacy of ‘seeding’ questions about society and politics that researchers may reflect upon. As a whole, discussions were useful to create an environment for discussion, for the contrasting narratives and ways of thinking about risk and the social value of science, as well as helping build trust and understanding. Nevertheless, having a record of these discussions proved difficult. I recorded all discussions except the first session because I was gaining the trust of the group and did not want them to feel intimidated by recording their interactions. I used a digital audio recorder that I usually placed in the centre of the table of the room around which the laboratory sat. This meant that recording quality was not the best, because some voices were recorded either at a low volume, or not clearly enough (which made transcription difficult), and because in some instances the recorder captured background noise very intensely (i.e., in the case of an air conditioning unit). Overall, recordings were of enough quality to be transcribed, although missing some words every now and then. I transcribed the recordings of the transcriptions as described above, except for one discussion in which background noise made it too difficult to put together a cohesive text.

### **3.4 Data analysis**

In qualitative research the researcher is the instrument (Guest et al., 2013). Behind every method lies a variety of assumptions regarding the nature of knowledge and the phenomena under investigation, the processes through which human beings concretize their relationship to their world. As important as the method of choice is the interpretation of the data. I analysed the data holistically, giving importance to context. I coded all written data, that is,

classified it according to ideas, themes, topics, activities, and other relevant categories (Schensul, 2012). For Saldaña (2009: 3) a code is “a word or short phrase that symbolically assigns a summative, salient, essence-capturing, and/or evocative attribute for a portion of language-based or visual data.” Coding was performed with the aid of fit-for-purpose software such as *NVivo*, designed to support data analysis through “creating, applying, and refining categories: tracing linkages between concepts; and making comparisons between cases and events” (Schutt 2011: 350). Coded texts were analysed following a ‘grounded theory approach’ with distinctive coding categories (cf. Corbin & Strauss 2015). I re-coded the data several times and reassigned codes as they better fit the themes that emerged from the data. Software like NVivo is a powerful tool that offers data storage and organization, but the task of the analyst is to assign codes and find connections between them, which should reflect patterns and help build conceptual and theoretical coherence in the accounts provided.

### 3.5 Summary and conclusions

In this chapter I have described the rationale for the empirical data I collected for this thesis. Qualitative research approaches are well suited for the research questions I address in this thesis (see **Chapter one**) regarding what imaginaries lead the emergence of xenobiology? What are the values, narratives and imaginaries of xenobiology? How are imaginaries related to scientific practices and expectations? Is xenobiology a responsible discipline? Do xenobiologists aim to shift our understanding of life? These questions depend on how researchers see their world and engage with society as researchers. The nature of these question is both abstract and subjective, as it depends on reflection upon scientists as to how they coordinate and justify their efforts to advance an emerging technology. In short, the approaches I employ allow me to reach an approximation of the scientists’ experience in advancing knowledge while requiring legitimation (public acceptance) and resources. The picture or arguments I present throughout this thesis are inherently limited by what researchers choose to share with me, how much they reflect upon the issues I present, and the quality of the interactions and activities I observed in the laboratory and academic instances.

The use of tools or approaches of qualitative research must not be taken lightly. Researchers doing qualitative research could think of it as just ‘talking to interesting people,’ but it is more of an interpretative exercise to find meaning in discourses and actions. For this thesis I combined a variety of approaches, like participant observation, semi-structured interviews, group discussions, secondary sources and media, to try to get the best of each. The different approaches I employed responded to different needs. Semi-structured

interviews with researchers and other actors (like civil servants or biosecurity experts) allowed me to ask direct questions about their opinions about xenobiology, biosafety and society. Through participant observation I gained experience about what it means to experiment with xenobiology, and its materiality. The laboratory, as a place where expectations are formed, and imaginaries are shaped, provided an excellent ground to observe ‘xenobiology in the making,’ and to provide a vantage point from which to assess expectations and visions of the future of xenobiology.

Furthermore, because the laboratory has been conceptualized as a place where trajectories of a field can be influenced or steered (Doorn et al., 2013; Fisher, Mahajan, & Mitcham, 2006), and where social scientists and natural scientists collaborate and their work intersects (Balmer et al., 2015), I aimed to add another layer to this thesis by bringing normative questions about society into the laboratory, in line with RRI (Stilgoe & Guston, 2017). I brought different perspectives and questions about the role of science in society through various interactions with participants in the laboratory. My goal was to raise awareness about such questions and ultimately lead to increased reflexivity, which should result in improved capacities for anticipating the outcomes of xenobiology (Barben et al., 2008).

From the methodological approaches I employed, it is worth emphasizing the difficulty in establishing a relation of collaboration in the same hierarchy of power as a principal investigator in charge of running a laboratory. Before establishing a collaboration, there is work to be done to make researchers in the laboratory aware of possible issues that may arise –issues that would usually go unnoticed– such as issues of power, values and distribution in society that are not necessarily relevant when experiments are conducted but are an integral part of a responsible scientific ethos. Caution should be exerted when referring to a laboratory group as a homogeneous collective, where a single identity is performed.

The type of questions I addressed in this thesis deserve further reflection on the limits of the qualitative research tools I employed. In studying visions, narratives, and imaginaries, the nature of these abstract notions has much to do with what is revealed as with what is concealed. Particularly when exploring the connection between xenobiology and biocontainment, or how xenobiology seeks legitimization, I paid attention to what thoughts were camouflaged, what motivations were not shared and were explained with alternative perspectives. As an analyst, care must be exerted in treating data and conversations as performative, not only by analysing the content of the conversations, but how such content can be used to advance certain agendas or play a particular identity. My point is that qualitative data requires an effort to engage with collected data, analyse it from multiple vantage points and dig deep into the multiple meanings that researchers convey. Conducting qualitative research is an activity of paying attention and connecting the missing dots.

## 4. The sociotechnical imaginary of life unbound

### 4.1 Introduction

Whether new technologies influence our lives in ways that are beyond our control, defying a perceived natural order, depends on beliefs and meaning-making (Douglas, 1966). At a first encounter with xenobiology, what may result most intriguing for many is the potential of the field to radically reconfigure life in unknown ways, defying what is perceived as pure and natural. In this chapter I address the efforts that xenobiologists make in shifting the boundaries of life, expanding them to include organisms that are not DNA-based, and by doing so, shifting perceptions of what safety means in biology. I ask what is new in xenobiology and how it aims to reconfigure previously held boundaries between the natural, the non-natural, and machines; or how it influences our ways of thinking about living organisms and long cherished routines and rituals in the life sciences; in particular, how the unnatural is framed as ‘safe.’ MIT Anthropologist Stefan Helmreich has studied life scientists, asking in particular ‘how biologists think about limits’, who ‘scout out life at its boundaries.’ (Helmreich, 2011: 677). In the book *Alien Ocean* (Helmreich, 2008), Helmreich explores from an anthropological perspective how scientists perceive life in the depths of oceans. Exploring limits is useful because it relates to a concern about how transgressive xenobiology might be in its enterprise of redefining or expanding the boundaries between the biological and the artificial. Is xenobiology a novel endeavour? Does it need to justify itself? Is it a radical transformation of life, or the continuation of previous trends? The idea of limits is present in the work of Bernadette Bensaude Vincent, for example when she writes, “Synthetic biologists working in this field [xenobiology], are engaged in a systematic *exploration of the realm of the possible*, and only indirectly concerned with understanding life or coming up with profitable innovations” (emphasis added) (Bensaude Vincent, 2013: 29).

Thinking of limits invites us to think of life as subject to reconstruction by scientists, to reconfigure it in ways that would not be possible without human intervention and advanced technologies. Expanding the genetic chemistry of life is motivating for scientists because they address fundamental questions in biology at the same time that they get the thrill of doing what no one else has done. Much of the excitement that synthetic biologists derive from creating new molecules comes from the sense of crossing an implicit barrier imposed by evolution, which has been crossed since the beginning of molecular biology. If we are to develop a thorough understanding of responsibility in science and the social value of research, engaging with the motivations of scientists is paramount. A researcher from the laboratory I studied provided an excellent synthesis of what is exciting about xenobiology:

The fact of creating what doesn't exist, can we do it? Is it possible to create what seems impossible? To go where no one else has been before? And doing something we did not know we were capable of. I think it has to do with the fact that this is the basis of life.

Motivation has been discussed in terms of what actors behind a given technology aim to achieve, which may attend particular interests, and not those of the public, as in the GM controversy of the 1990s in Europe (i.e., Grove-White et al., 1997; Grove-White et al., 2000). A major concern for scholars is the 'purpose' of innovation, which is often occluded by a dominant institutional discourse of risk (Wynne, 2002). Authority and power in science is not just about who commands but why. Understanding how scientists see themselves, or what they identify themselves with, is important to understand the choices they make and the trajectories they follow in building a discipline or advancing new metaphors and visions of life. This also includes the role of myths such as a 'golden age' in which academics had more freedom and time to pursue their own intellectual interests (Holden, 2014).

Shifting metaphors about life, from life as an organic unity, to life as information, seem destabilized by the creation of novel forms of life in xenobiology. It is necessary to question how they relate to previous epistemologies, like in molecular biology (cf. Knorr-Cetina, 1999), which gives primacy to genetic reductionism. What I refer to as xenobiology comprises a common agenda of developing alternative genetic systems to DNA as an information storage molecule (i.e., Xeno-Nucleic Acids), recoding the genetic code (reassigning the correspondence between a DNA codon and a given amino-acid), and inserting non-canonical (not produced by natural organisms) amino-acids into proteins, or other types of molecules or functional groups<sup>62</sup> (**Chapter one** and **Appendix one**). In the laboratory I studied there were no 'xeno-organisms,' or (micro)organisms fully based on XNA as its genetic storage molecule, they are still in the making, far from becoming black-boxed. I propose in this chapter that it is convenient to think of xenobiology in terms of the attitudes, values and ways of thinking about life that scientists incorporate in their experiments.

Scientists defy what is biologically possible as a form of *limits*. A useful way of understanding how xenobiologists fabricate nature in the laboratory is thinking that *life is what we make of it*. As xenobiologists recognize the flexibility of life as the result of processes of evolution that could have been otherwise, they justify their work as *experiments in evolution*, of adding new constituents to a repertoire of living organisms that is ever changing, in the process of life and death that all species are subject to. For some people, the interest in bringing novel biological organisms to existence may seem transgressive. Transgression goes

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<sup>62</sup> As explained in **chapters one** and **two**, important studies that have guided much of the analysis in this thesis include Malyshev et al., 2014; Mandell et al., 2015; Rovner et al., 2015. Not all practitioners of xenobiology-related affairs use the label of 'xenobiology'.

beyond what is acceptable or according to the cultural norms of a society, as Sheila Jasanoff writes:

Because genetic engineering transgresses some of the most deeply entrenched categories of Western thought, the institutions that promote and regulate biotechnology are particularly likely to be involved in the production of novel ideas, norms, and meanings (Jasanoff, 2005: 28).

In this chapter I suggest that legitimation and justification for research in xenobiology is required, and I provide an overview of rhetorical moves to accomplish this. I first consider in **Section 4.2** the argument that xenobiology constitutes an effort in redefining life, in terms of its boundaries and what is biologically possible. I expand on the use of the term limits, as xenobiologists approach life as plastic and in terms that can be modified and reconfigured. **Section 4.3** provides an overview of conceptual and symbolic tools that enable sense-making in the production of new knowledge and the definition of identity of xenobiology, of which I emphasize the importance of evolutionary thinking for establishing a point of reference from which xenobiologists explore new biological worlds. **Section 4.3.1** explains the rhetorical move that the natural world is limited in terms of the solutions it can provide for meeting social ends, hence it is necessary to explore biology at its boundaries to find much needed solutions.

Next, **Section 4.3.2** puts into question the hegemony of DNA as the molecule of life, to suggest that the radicalness of altering the genetic basis of life depends on cultural icons of biology in a society. In **Section 4.3.3**, instead of analysing conceptual and symbolic tools, I introduce the vision of developing XNA-based microorganisms, suggesting that we should enquire about where is the biological in xenobiology, as a strategy to question motivations of the field and associated justifications like the pursuit of safety-by-design. Last, in **Section 4.3.4** I explain the logic of molecularization, of seeing biological systems as components that can be detached and aggregated in various ways, stripping them from their original historical and biological context.

Having provided an account of shifting ideas about life, I return to the notion of limits to interrogate the terms under which xenobiologists claim that biology is safer the more unnatural it becomes. This claim is backed by what I call the imaginary of life unbound, thinking that the parameters with which we understand life are changeable and unstable, as I elaborate in **Section 4.3**; **Section 4.4** explains that part of the work involved requires positioning xenobiology as a safer option than its natural counterparts. In **section 4.4.1** I detail the metaphor of navigation and exploration of a 'virtual continent of life' that Philippe Marlière has put forward, examining themes of distance between continents that make sense when seen through evolution. These metaphors have performative power in motivating research in the field and creating a space for safety that only xenobiology can occupy.

Navigation and exploration are connected to safety, as I show in **Section 4.4.2**, because unnatural biological systems, *distant* from the natural DNA-based world, do not share the same genetic foundations and hence are safer. At the same time unnatural biological systems constitute a ‘safe space for experimentation,’ where considerations of governance would not normally apply. I finish the discussion by analysing in **Section 4.4.3** the relationship between exploring life at the limits of what is biologically possible, and the responsibilities and duties that scientists acquire in doing so.

## 4.2 Redefining life, expanding limits

In this section I expand on the argument that xenobiology constitutes an effort in redefining life, in terms of its boundaries and what is biologically possible. This involves scientists challenging decades-old assumptions by imagining that life could function with a genetic system not based on DNA. The meaning or logic of life then changes to be the result of evolutionary contingencies, finding biotechnology-based applications outside natural diversity, and more importantly, thinking of life as what is biologically possible, not what is biologically given. These ideas are commonly held in the life sciences, and predominantly in synthetic biology communities. As such, even though they might not be exclusive views of xenobiologists, they are important to introduce metaphors and narratives that are associated with xenobiology, such as departing from nature, or having organisms work with XNA compounds. In what follows, I highlight the importance of imagination in thinking about the multiple possibilities of life. I suggest throughout this chapter that xenobiologists aim to persuade the public that life is more flexible than we are used to think of. If scientists collectively think that life’s boundaries are elastic, referred to as ‘imaginary of life unbound,’ this carries along ramifications for how scientists think about experimentation in the laboratory and with society when release of microorganisms to the environment is intended.

I use the term ‘*limits*’ as a device that may help to understand the worldviews of xenobiologists. As Philippe Marlière has stated, xenobiologists should “*accept no limits*,”<sup>63</sup> — hence the title of this thesis. Thinking of limits involves two aspects. First, it reflects a view of life (in the sense of biological beings or organisms) as subject to definition, to categorization, to classification; it is inherently arbitrary. Life is subject to discrete categorizations as different from death, from the inert, or from life that did not originate in this world. Helmreich (2008) entertains this idea in his book *Alien Ocean* where he considers

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<sup>63</sup> Philippe Marlière. Lecture titled ‘Accept no Limits’. Conference on Cellular and Molecular Biotechnology, held in *Institut des Hautes Études Scientifiques (IHÉS)* in Paris, in December 2015. Available in YouTube: [www.youtube.com/watch?v=D8X9hz2MdZs](http://www.youtube.com/watch?v=D8X9hz2MdZs) [last visited January 11, 2018].



life in deep oceans as something different from life in more familiar environments. His work also involves studying life in other connotations, such as *in silico* life —simulations of algorithms that behave like living, evolving organisms— or life in extreme environments, like near volcanoes or hot springs.

The literature in bioethics has addressed the idea of limits, mostly aiming to establish limits that are not to be crossed, or checkpoints, which bioethicists carefully monitor<sup>64</sup>. Research in xenobiology does not have profound ramifications for the manipulation of human beings, in contrast with novel advances in medical genetics (Jasanoff, 2016; Rose, 2006), generating a different set of questions. For Nikolas Rose, vitality is at stake with new genetic technologies: “At the level of the organism, where the very meaning and limits of life itself are subject to political contestation.” (Rose, 2006: 49). Thinking of limits invites us to think of life as mercurial, a construct in constant (re)negotiation. Scientists think of life in terms not in terms of a given, stable construct, but a category that is defined through what is biologically possible, not by normative aims, such as what should be done, or how nature should be treated (and what is imagined). Second, thinking of ‘limits’ is useful for studying science in public, as the question revolves not around what is biologically possible, but what *should or should not* be done with living organisms. Simply put, asking whether there is a limit that should not be crossed when altering the natural order, which people may consider transgressive. If we are to understand xenobiology as a way of thinking and handling materials related to life, then crossing limits is a key component of such thinking. Alternatively, we need to examine whether a better notion is *expanding limits*, as opposed to crossing them. The project of xenobiology comprises enlarging the possibilities associated with life.

For xenobiologists it is useful to think of a continuum of life which is being stretched, or amplified, when they expand the repertoire of nucleic acids and amino-acids that organisms use to perform tasks. Many scientists I spoke to hold this position, sceptical of treating natural organisms as different from genetically modified ones. Some argued that humans had been modifying animals and crops since several millennia ago, and conducting genetic engineering was but an obvious, subsequent step in a chain of steps of humans intervening in the natural order. I addressed this subject with a researcher in the lab I studied, who expressed that they did not feel like xenobiology was testing existing definitions of what counts as natural. In our conversation, the researcher invoked the breeding argument, according to which humans have conducted genetic engineering for thousands of years ago by selectively breeding plants and animals. In this line of thinking genetic engineering is a

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<sup>64</sup> For some studies on ethical aspects of synthetic biology, see Bedau & Parke, 2009; Deplazes et al., 2009; Dymond, 2016; Hagen et al., 2016; Newson, 2011; Rabinow & Bennett, 2009.

shortcut, a way of manipulating life within many paths that are equally valid. For a living entity to be ‘alien’ or ‘foreign’ to life on Earth, it would have to come from another planet, according to the researcher. This worldview about nature and the synthetic makes it difficult to sustain meaningful conversations about whether xenobiology pushes limits, since the conversation turns around arguing whether there is such a thing as the natural and the unnatural in the first place, and what are the fundamental principles of life. For Phillipe Marlière, in an interview about the achievement of Floyd Romesberg lab in 2014,<sup>65</sup> biology does not fully reflect the fundamental properties of life. Scientists, then, want to know what is at the core of living organisms. He said the following:

Biology has hitherto studied living beings as found in nature, whose recipe of manufacture is written with the genetic alphabet ACGT. To ask oneself *what is really essential in the conception and design of an organism*, in the sense in which engineers understand it, has hitherto been considered as a marginal issue outside the field of serious research.

Thinking of limits involves imagination as scientists think of xenobiology as experimentation with a fluid life. In the ethnography of synthetic biology laboratories of Caitlin Cockerton (2011), she suggests that developing new technologies requires “dreaming up ideas”, an “imaginative exercise in the mind” (ibid., p. 303), and requires tools for thinking, that allow sharing, dissemination and refinement of ideas. She highlights writing practices (on black-boards, drawing pictures, creating graphs and charts).<sup>66</sup> The question in xenobiology concerns not only the limits of what is possible, but also what separates objects. Limits help to think of genetic information as being divisible, separable, but at the same time, genetic information is being compartmentalized, part of a spectrum that encompasses all living organisms. As interviewee 6B explained that “one of our major pitches [in grant applications] is that by creating XNA-based life, you can separate things. Separate genetic information.” Furthermore, it is useful to think of limits both as material, in terms of what is biologically possible, and in terms of what scientists *imagine* is possible, for whom biology is much about what living organisms are made of, but also about what they could have been made of.

In accordance with the metaphor of *life as information* in molecular biology, limits in xenobiology are framed as the transfer of genetic information in biology (Kay, 2000). The website of the laboratory of synthetic biologist Vitor Pinheiro echoes this impression.<sup>67</sup>

Despite biology’s immense diversity, on some cases biology has provided us with a single answer. One such example is the storage and propagation of chemical information, where DNA and RNA are the only genetic materials, and the genetic code is universal. *My view is*

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<sup>65</sup> See footnote 10.

<sup>66</sup> In my fieldwork I also encountered the use of drawings when a researcher in an XNA-related project explained to me the experiments they were conducting, they used to make drawings to explain the selection platforms being developed. To me such diagrams were of little use but were the language the researcher used to communicate their ideas.

<sup>67</sup> From <https://vbpinheiro.wordpress.com/research> [last visited February 2, 2017].

*that biology has not (and cannot have) explored all possible solutions to any given problem.* Simply put, as an evolutionary process, biology is extensive but not thorough (Emphasis added).

Hence, imagination is linked to exploration –filling the blanks that nature and evolution have left. The recurrence in xenobiology to abstractions like the universality of the genetic code, or the exploration of evolutionary processes are a feature of imagination. Highlighting the role of imagination in thinking about xenobiology, 9A commented:

We are trying to see *what we can get away with*, which raises more questions, and people do more investigations, and this just takes science forward, because there are so many things you can't rationally think about but are more discovery oriented; you just land upon some things which people did not land upon because probably they didn't ask those questions.

Interviewee 9A refers to the possibilities of manipulating life in the laboratory, which inevitably lead to roadblocks. '*Getting away with*' captures the thrill for scientists who conduct research in the life sciences, who are unsure of whether their attempts to intervene nature will work. To overcome roadblocks, asking the right questions is essential, it is part of experimentation. At the same time, 'getting away with' (although not implicitly stated by 9A) can be interpreted as challenging what society may deem as acceptable in biomedical research –I address this theme in **Chapter seven**. Arguably, xenobiology is also about the kinds of questions that are asked, which in turn push a specific research agenda and goals. Thinking of limits can be defined in terms of asking whether there is a limit to what is *doable*. 8B encapsulates this idea by commenting "There's always the question of –have we gotten this far as we can? or is there a lot more that can be achieved? Assuming there is, then that's where I kind of see the field standing now, on the cusp of being broadly useful." Put in this way, thinking of limits is defined by *what is possible*: what scientists can get away with in the biological world.

The attitude toward limits that I describe detaches developments in the life sciences from consequences for social arrangements; thinking about limits is tied to thinking about the arrangements that enable that they are challenged. Such profound transformations not only put into question the genetic constitution of living organisms, but the ways in which we understand life, think about nature, and give meaning to our experience in the world. In what follows, I provide an overview of some foundations of biology and cultural artefacts that are important to understand the narratives, visions and imaginaries of xenobiology, particular when it comes to the imaginary of 'life unbound,' in which life is seen as malleable, and subject to imagining what is biologically possible.

### 4.3 Reimagining biology

Expanding further into how xenobiologists think about limits, they draw on paradigms and cultural resources from the life sciences, conceptual and symbolic tools that enable sense-

making in the production of new knowledge and the definition of identity of an emerging discipline. Researchers in xenobiology use these resources to imagine life in a different way and justify research in their field. These operations and transitions in how researchers think about biology provide a solid ground on which to assess the imaginaries and visions that drive the development of the field: they make the unnatural seem more natural. Visions of what biology can accomplish also incorporate visions of how the field should be governed.

Xenobiologists seek to prompt a redefinition of life that expands the barrier of what is possible in biotechnology, or as Markus Schmidt recently titled a presentation<sup>68</sup>: ‘Encountering Other Forms of Life.’ As Steven Benner (2003: 118) writes, “Life is a special kind of chemistry”, possessing “an uncommon property (the ability to direct the synthesis of self-copies), in a way that allows transformed molecular structures themselves to be copied.” Highlighting the role of imagination, Benner and colleagues also ask:

Can alternative chemical structures support rule-based molecular recognition as well? To answer these questions requires that *alternative structures be imagined*, and that the power of contemporary synthetic organic chemistry be applied to prepare them in the laboratory (Emphasis added) (Benner et al., 2003: 125).

Imagining alternative genetic systems and their accompanying discourse and rhetoric that proponents of the field developed has roots in foundations of the life sciences such as evolutionary theory. Researchers in the life sciences admire evolutionary biology. This analysis will be useful later in the chapter when I refer to safety in terms of an evolutionary *distance from the natural world*. I go into detail on aspects of evolutionary theory because the concept of limits and the departure from nature that xenobiologists propose is better understood in terms of seeing biology as the result of an evolutionary history.

### 4.3.1 Biology is limited

To explore the limits of the biological world, scientists argue that biology or ‘Life on Earth’ is *limited* as a source of solutions for major challenges humanity faces. In what follows, I explain that synthetic biology takes distance from approaches in biotechnology that seek to extract value from molecules and organisms already found in nature. This sets an important distinction between xenobiology and synthetic biology.<sup>69</sup> In the latter, some of the most important achievements so far have been the production of chemicals already found in

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<sup>68</sup> Blumberg Symposium at the Library of Congress. Life as it Could Be: Astrobiology, Synthetic Biology, and the Future of Life. Xenobiology: Encountering Other Forms of Life. 28 September 2017. Washington DC, USA

<sup>69</sup> Questions about metabolic engineering had a space in the second xenobiology conference held in Berlin in 2014, under the session themes of ‘biosynthesis’, or ‘carbon fixation’, which reflects the wide degree of themes that fall under the field of xenobiology.

nature,<sup>70</sup> such as artemisinin (an anti-malarial drug found in the tree *Artemisia annua*) in *E. coli*<sup>71</sup> and yeast;<sup>72</sup> and the chemical vanillin.<sup>73</sup> However, biotechnological solutions based on the existing repertoire of nature are part of an active field of research, for instance the discovery of useful compounds (e.g. therapeutics and enzymes) in microorganisms (Bull, Goodfellow, & Slater, 1992; Bull, Ward, & Goodfellow, 2000). Such organized activities, many of which fall under ‘bioprospection,’ have been the subjects of biotechnology policy, such as the ‘Cartagena protocol’ and its associated discussions on biosafety, and are the result of the recognition that biodiversity is a source of value that needs protection from trade (Bail et al., 2001).

The notion that biology is limited or insufficient for providing biotechnological applications has different layers. The website of Isthmus, a biotech company founded by Philippe Marlière, a text about first xenobiology conference (XB1)<sup>74</sup> promotes the field as an ‘emancipation’ from nature: “Xenobiology (XB) is the endeavour to *overcome the constraints* imposed by evolution on natural living organisms”<sup>75</sup> (Emphasis added). This suggests disenchantment with the natural world, and a necessity to break free from it. Protein engineer Frances Arnold (Nobel Prize winner for Chemistry in 2018), during an interview for the magazine *ChemViews* in 2011, explains,<sup>76</sup> “Natural organisms have evolved to survive and reproduce, not to solve human problems such as making renewable fuels or medicines. So, if we want to reprogram organisms to do that, we have to re-write the DNA code to tell them how.” Synthetic biologist 19A elaborates this argument further, explaining the importance of the use of unnatural amino-acids in protein engineering:

There are limitations in terms of the chemistry that you can do. ... putting unnatural amino-acids it might allow, or will allow, because the chemistry, some chemistries will do, will allow novel reactions to take place. So, you could design enzymes that then have additional activities, that no enzyme yet has.

Biology is a field of enquiry not centred around laws but historical contingencies, accidents that shaped the evolutionary history of all living organisms (Keller, 2007). Surpassing the limitations imposed by evolutionary processes is an extremely appealing challenge for researchers involved in xenobiology. The prominent evolutionary biologist

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<sup>70</sup> Issues around social justice have been a target for critique of synthetic biology by civil society groups (cf. Stemerding et al., 2009).

<sup>71</sup> See Martin et al., 2003.

<sup>72</sup> See Ro et al., 2006.

<sup>73</sup> See <http://www.evolve.com/vanillin/> [last visited 7 April 2017]; also see comment from Friends of the Earth, [http://www.foe.org/system/storage/877/a2/1/4914/issue\\_brief\\_-\\_synbio\\_vanilla.pdf](http://www.foe.org/system/storage/877/a2/1/4914/issue_brief_-_synbio_vanilla.pdf) [last visited 7 April 2017].

<sup>74</sup> See footnote 5.

<sup>75</sup> <http://www.isthmus.fr/?p=86> [last visited 30 March 2017].

<sup>76</sup> In an interview for the magazine *ChemViews*, by Vera Köster. See [http://www.chemistryviews.org/details/ezone/1376211/Interview\\_with\\_Frances\\_H\\_Arnold\\_Design\\_by\\_Evolution.html](http://www.chemistryviews.org/details/ezone/1376211/Interview_with_Frances_H_Arnold_Design_by_Evolution.html) [last visited 30 March 2017].

Theodosius Dobzhansky wrote a famous essay in 1973 titled ‘Nothing In Biology Makes Sense Except in the Light of Evolution,’ a motto that still gains currency. Even molecular biology pioneer Sydney Brenner wrote in a 1974 report to the Ashby committee<sup>77</sup> (more in **Chapter five**), the first British committee to assess the implications of recombinant DNA technology (quoted in Wright, 1994: 75-76):

It cannot be argued that this is simply another, perhaps easier way to do what we have been doing for a long time with less direct methods. For the first time, there is now available a method which allows us to *cross very large evolutionary barriers* and to move genes between organisms which have never had genetic contact (Emphasis added).

This reflects an inclination to think of limits as ‘evolutionary barriers’ early in the beginnings of genetic engineering. Once it has been established that solutions are to be found in synthetic approaches, far from nature, then a universe of possibilities is open. Solutions have to be sought elsewhere, not in the natural world as currently known. In summary, experimentation in xenobiology needs a point of reference, a starting point according to which biotechnology-based solutions are not to be found in nature but need to be created.

### 4.3.2 DNA as the molecule of life

Part of the novelty of xenobiology is the move of thinking outside the limits of what biology can be made of (in terms of its genetic constituents). In this section I briefly illustrate the importance that both scientists and the public give to DNA as the basis of life, which partly explains why research in xenobiology may seem transgressive; the high position given to DNA is a historical and cultural outcome. If we accept that DNA is not the foundation of life and biology and invert the question to value other properties of life –metabolism, robustness, etcetera– then the project of creating alternative genetic systems may not seem as radical. Imagining that life could have been different opens the door for a new range of possibilities in the life sciences. Although experimentation with alternative forms of nucleic acids took place in the 1960s, these efforts were abandoned to focus on DNA. One of the reasons why xenobiology has come to fruition in the last decade, with initial efforts in the late 1980s, is because available tools (i.e., enzymes and techniques) had not been developed until recently.

The intention to developing genetic systems based on a different chemistry or reconfiguring existing genetic systems may seem revolutionary because we are fascinated with DNA as the molecule of heredity, and we are used to the idea that DNA is central to what we conceive as life. This owes to the history of molecular biology, which has been

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<sup>77</sup> “Evidence for the Ashby Working Party”, paper submitted to the Working Party on the Experimental Manipulation of the Genetic Composition of Micro-organisms, 26 September 1974, RDHC.

written magnifying discoveries about the genetic code. For historian of science Evelyn Fox Keller, molecular genetics centred around the structure and function of DNA, capturing the imagination of scientists; she highlights the importance of DNA by calling it the ‘master molecule’ (Keller, 2000: 54). But the fascination with DNA extends to the genetic code and the ‘central dogma of biology.’<sup>78</sup> In the book *Who Wrote the Book of Life?: A History of the Genetic Code*, Kay (2000) interrogates the metaphor of the genetic book of life and its informational and linguistic attributes. Her book describes the transition in molecular biology to the ‘information discourse’ derived from mathematical communications theory. She claims that the discursive framework endured because it had ample operational utility; however, the idea of a code and its associated metaphors were applied inconsistently, and their original meaning changed when adapted to molecular biology. By the 1960s the genetic code was viewed as the ‘arbiter of genetic information, the central problem of molecular biology’ (ibid, p. 329). I quote Susan Wright (1994: 67) at length because her summary of breakthroughs that gave rise to molecular biology is useful for the discussion that follows:<sup>79</sup>

The main concepts underlying this tradition –that genes consist of DNA and that DNA encodes information determining the process of replication and protein synthesis– were of course embodied in the model of DNA proposed by James Watson and Francis Crick in 1953. Two decades of research based on the Watson–Crick model produced dramatic theoretical and technical achievements. The genetic code was deciphered; the cellular machinery responsible for replication of DNA and protein synthesis was described in considerable detail; the biochemical pathways involved in replication, expression, and natural recombination were defined ... These theoretical advances were reflected in new and impressive capacities to manipulate DNA.

The importance of DNA in molecular biology is such that genetic engineering and molecular biology are built on the foundations of the discovery of the double helical structure of DNA and the deciphering of the genetic code. Recombinant DNA technologies that were developed in the 1970s and soon after sparked a booming biotech industry, were based on the insertion of DNA segments into different species. To modify life became associated with modifying DNA. Even the revolutionary technique of PCR, as a concept, came from the idea of taking DNA out of its context (Rabinow, 1996). As Nikolas Rose explains, an informational epistemology took place in biology in the 20th century. Rose (2006: 44) quotes a translation of Georges Canguilhem (1994: 316-317), contemporary biology has favoured:

The vocabulary of linguistics and communication theory. Messages, information, programs, codes, instructions, decoding: these are the new concepts of the life sciences.... The science of life no longer resembles a portrait of life ... and it no longer resembles architecture or

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<sup>78</sup> Kay (2000: 329) attributes Francis Crick for the label ‘central dogma of biology’, which consists of the unidirectional flow of information from DNA to RNA to proteins. She cites Francis Crick, ‘On Protein Synthesis’, in *Symposium of the Society for Experimental Biology*, 12, p. 138-63. New York: Academic Press. 1958.

<sup>79</sup> For accounts on the development of molecular biology in the 1950s and 1960s, see Allen, 1975; Freifelder, 1978; Haynes & Hanawalt, 1968.

mechanics... But it does resemble grammar, semantics and the theory of syntax. If we are to understand life, its message must be decoded before it can be read.

At the epicentre of this epistemology DNA takes the stage as the molecule of life. The belief in DNA as the basis of life gave rise to the Human Genome Project, with the strong belief that establishing the sequence of DNA letters in humans would give rise to a plethora of medical therapies and far-reaching applications. However, the Human Genome Project was entangled in scientific and political issues (Balmer, 1996; Cook-Deegan, 1994) and has provoked a paradigm shift in genomics and biotechnology (Glasner, 2002). DNA has also become a 'cultural icon' (Nelkin & Lindee, 2004) and has been used in science policy circles as a metaphor to describe the relations between university, industry, and government, as a triple helix (Etzkowitz & Leydesdorff, 1998). The double helix is widely recognized, being used in the logos of biotech companies and science parks, often becoming synonymous with innovation. DNA has also become a metaphor to signify culture, with established practices, customs, behaviours and ways of relating among individuals.<sup>80</sup>

In summary, given the position of DNA as the molecule of life and its penetration in scientific and popular culture, the goal of xenobiology of constructing novel organisms based on alternative genetic chemistries may seem transgressive. Xenobiology is being built in a scientific culture that highly values life as associated with DNA. As xenobiologists aim to redefine the boundaries of life, they open the door to question the predominance of DNA. This is exemplified by interviewee 17A, a synthetic biologist who focuses on metabolic engineering. In his words, "I see first and foremost the phenomenon of *life as a phenomenon of metabolism*, much before talking about any kind of DNA information storage and so on, the actual basis of life is metabolism, that's the centre" (emphasis added). Or as science journalist Michael Marshall would have it, 'DNA has no reason to feel special.'<sup>81</sup> Accordingly, if we give less predominance culturally to the importance of DNA, then manipulating the genetic code as xenobiologists propose might not be as transgressive as it might sound in the first place. Reimagining the role of DNA yields opportunity for rethinking life at its limits.

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<sup>80</sup> See, for example, Bonchek, M. (2016, December). How to Discover Your Company's DNA. *Harvard Business Review*. Retrieved from <https://hbr.org/2016/12/how-to-discover-your-companys-dna> [Last visited 2 November 2018].

<sup>81</sup> Marshall, M. 2012. DNA has no reason to feel special. *New Scientist*, 19 April. Retrieved from: <https://www.newscientist.com/article/dn21720-move-over-dna-six-new-molecules-can-carry-genes/#.VJGvi14gKB> [last visited July 24, 2018].



### 4.3.3 The biology in xenobiology

A theme that emerged in my interactions with scientists questioned the *biological* aspects of xenobiology. This leads our attention to the activities that could make xeno-organisms a reality, in addition to the justifications that are mobilized for developing *safe* xeno-organisms. The absence of the biological in xenobiology hints the processes before xenobiology becomes black-boxed. In this chapter, interrogating ‘limits’ prompts to ask in what terms are limits being overcome. Xenobiologists pursue the development of *in vivo* organisms that can function with altered genetic systems, based on XNA nucleotides or a reconfigured genetic code. This step of moving from *in vitro* to *in vivo* marks a milestone for the field, becoming an ultimate goal. It has served as a common challenge to match by researchers in xenobiology. For instance, Malyshev & Romesberg (2015b: 11941) wrote “the most exciting application of UBPs [unnatural base pairs] is their use for the creation of semi-synthetic organisms that store and retrieve increased information.”<sup>82</sup> Moreover, for Farren Isaacs of Yale University, commenting on the work of Pinheiro and colleagues (2012), stated that “the immediate question is whether these XNAs can be introduced into cells.”<sup>83</sup> When I asked interviewee 5C about the goal of using unnatural base pairs *in vivo*, he commented that:

What I’m most interested in is going into an organism. In fact, I’m not that interested in unnatural base pairs. ... from the very beginning though, my interest has been focused on organisms, on biology... there’s no project that I care emotionally more about than my [research project in xenobiology].

He then added that moving to *in vivo* is “an obvious goal.” He added,

You don’t have to be a rocket scientist to see that. If you’re designing unnatural base pairs, well, what are base pairs used for? Well, they’re predominantly used to code for information in cells. So, could we use them there? That’s an obvious sort of question to ask.

Moving from *in vitro* to *in vivo* XNA-based organisms is exciting for scientists. For example, interviewee 6B commented, “If you ask many of the researchers in the consortium ... if you could pick one thing that you are interested in about this project, what would be?— I mean, they will probably tell you that is to basically *figure out if life can be built in other ways.*” (Emphasis added). Likewise, another way to understand the transition to living organisms is that for synthetic biologists, synthesis serves as a way to understand life (Benner et al., 2011); building serves as a path to better understand essential processes in living beings.

The experiments conducted in the laboratory I studied were *in vitro* assays, oriented towards the design and development of new enzymes. The question of moving XNA from *in vitro* to *in vivo* was present as a long-term goal. It serves as a form of imagination that guides

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<sup>82</sup> This defines a research line of Romesberg lab (Feldman & Romesberg, 2018).

<sup>83</sup> Marshall, M. 2012. Move over DNA: Six new molecules can carry genes. *New Scientist*, April 19, 2012. Retrieved from: <https://www.newscientist.com/article/dn21720-move-over-dna-six-new-molecules-can-carry-genes/#.VJGvi14gKB> [last visited July 26, 2018].

experiments. This is exemplified by an episode in a weekly laboratory meeting, in which a laboratory member presented ‘work in progress.’ Referring to the goal of designing and building [*XNA machinery*], the researcher explained that such goal could be approached from three perspectives: first, for the synthetic biologist, it would be a question of ‘efficiency’ and orthogonality; second, for a molecular biologist, a challenge of replicating double stranded XNA from single stranded XNA, which had been accomplished *in vitro* but not *in vivo*; and third, a challenge for the virologist. During the presentation, and in other presentations I observed that researchers focused on how to get there.

If we situate xenobiology in a spectrum between the *in vitro* and the *in vivo*, some researchers think of the field as being mostly chemistry based. A laboratory member commented that in the XB1 conference, the bulk of the talks were based on chemistry, also adding,

You always need the support of a living platform, like bacteria. But so far, we are in a stage of chemistry, that, a project that is built from the bottom up, not top down. The idea is to start with the basics, start building the machinery, that will give place to an *in vitro* system, which later on can be transferred to an *in vivo* platform. For now, we are one hundred percent in the chemical stage.

This is line with the assertion of a researcher who commented that there is *no biology in xenobiology*. Interviewee 5C expressed that the “state of the art, mostly, on xenobiology, is designing unnatural nucleotides. And replicating them *in vitro*. Or not even replicating them, just building them, or trying to get them to replicate. People like [name of researcher], who’s done great work, don’t get me wrong. But that’s not biology. There’s no cell there, there’s no living thing there.” 5C reflects a vision that xenobiology should be *in vivo*, where the field is headed. Nevertheless, some studies have featured the incorporation of non-natural nucleic acids *in vivo* (Malyshev et al., 2014; Malyshev & Romesberg, 2015a; Marlière et al., 2011; Zhang et al., 2017). Regarding Marlière’s 2011 milestone study in which an *E. coli* strain was made to depend on the synthetic compound chloro-uracil (**Appendix one**), interviewee 17A explained that this related not so much to the goal of incorporating alternative nucleic acids into a cell, but as a way of controlling a cell (which leads to safety).

You’re probably aware of his work on the chloro-uracil. So, we already have an organism that is completely dependent on XNA. So, we are there in this regard. Philippe’s idea in this sense is not to use this organism to create or to support novel activities that do not exist in nature, but rather to create an organism that is completely confined into synthetic habitats, so there will be no spillover of this organism.

Noteworthy, advances in xenobiology *in vivo* have been reported, which raises questions about the need for safety features. For 17A, this is a reason for having XNA-based organisms is the capability of tightly controlling organisms. This begs to ask, what comes first? Does xenobiology lead to safety? Or does the search for safety and control leads to xenobiology? Part of the task of studying xenobiology is identifying competing motivations for the field,

and justifications that may conceal different motivations. Some goals in xenobiology are ‘sold’ as applications, when they may serve as steps closer to an XNA-based organism. Distinguishing between motivations for conducting research and seeking applications is difficult. For example, interviewee 14A considers that unnatural nucleic acids must ‘do’ something, or have a function, “Right now, [unnatural nucleotides do not] do anything. It’s just being replicated inside of the cell. The ultimate goal is to have it used to encode proteins to actually encode the incorporation of unnatural amino-acids.” The connection between applications and a living platform (or organism) is also highlighted in the website of XENOME, a project in which Philippe Marlière and Piet Herdewijn participate, based in the Institute of Systems and Synthetic Biology of Genopole in France. According to the project’s website,<sup>84</sup>

The ultimate aim of the XENOME team is to design and engineer novel cellular components to elaborate safe GMOs (genetically modified organisms) whose *in vivo* generation and functionality can be strictly controlled, and which therefore allow the development of new and advanced applications in biotechnology.

This quote illustrates the tension between the motivation to achieve an XNA-based organism, applications, and understandings of safety. Safety can serve as a vehicle to conduct highly motivating research in the field and given a sociotechnical imaginary of ‘controllable emergence’ that both scientists and science funders share (**Chapter six**), appealing to safety can enable the advancement of xenobiology. For instance, the European funding body ERANet selected in its second call for projects like ‘*in vivo* XNA —Orthogonal biosystems based on phosphonate XNAs’ and ‘TNA episome —Design and Synthesis of a Bio-orthogonal Genetic System Based on Threose Nucleic acids *In Vivo*,’ which have in common that they aim to develop *in vivo* features.

Nevertheless, such hype about xenobiology and its potential once *in vivo* organisms have been conquered does not go unnoticed. After praising xenobiology’s concern with nucleic acids, then 17A questioned its usefulness, “It’s a really interesting kind of topic, but regarding its applicative side, you really need to ask the XNA people, because *I fail to see what’s so exciting about it*” (Emphasis added). XNA-based organisms are far from a reality. For our purposes and the scope of this thesis, it helps to think of xenobiology as an idea —an attitude to redesigning life— more than an actual reconfiguration of life taking place. The visions and imaginaries behind xenobiology need to be understood in the context of the scientific practice that supports them and the practices they aim to change, in redefining the boundaries of the genetic basis of life.

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<sup>84</sup> From <http://www.issb.genopole.fr/Research/teams/xenome> [last visited April 3, 2017].

#### 4.3.4 The logic of molecularization

I have suggested that much of the novelty about xenobiology lies in its imagination of life, creating a particular scientific identity. A third element in this discussion about the foundations and cultural artefacts of biology is important for the rhetoric of safety that xenobiologists create by shifting long held categories of life and the natural. I interpret the transformation of the notion of life from a material body to the circulation of information that is subject to evolutionary pressure as the decontextualizing of life, a biological epistemology. As organisms or biological systems are decontextualized or molecularized, or even disassembled, thinking about novel relations between the resulting components becomes easier. Led by metaphors of ‘life as *exploration*,’ instead of ‘life as information,’ the requirement for scientists is not the isolation and characterization of the molecular components of genetic systems, but their creation and mimicry from already discovered (and partly understood) processes. The core of xenobiology consists of developing new enzymes that do not exist in nature, such as polymerases, and creating a cellular machinery that can function with non-natural components like nucleic acids and amino-acids. For xenobiology, throughout the challenges of assembling XNA-based organisms, the living organism is molecularized, as their components and cultural meanings are lost in the processes of creating new components of artificial genetic systems. Such systems do not require an immediate connection between a genetic system and a cell (or a body), but can exist separately, detached from living organisms with which we would share some similarity by sharing the same genetic code or genetic material.

The logic of molecularization is one among the five ‘pathways’ that Nikolas Rose (2006) identifies in his book the *Politics of Life Itself*, a ‘style of thought’ (following Ludwik Fleck) that envisions life at the ‘molecular level.’ I find the following description the most suitable for our purposes:

Molecularization strips tissues, proteins, molecules, and drugs of their specific affinities— to a disease, to an organ, to an individual, to a species—and enables them to be regarded, in many respects, as manipulable and transferable elements or units, which can be delocalized— moved from place to place, from organism to organism, from disease to disease, from person to person (ibid, p. 5).

Rose adds, “molecularization is conferring a new mobility on the elements of life, enabling them to enter new circuits—organic, interpersonal, geographical, and financial” (ibid., p. 15). According to Rose, this style of thought has had repercussions for how the life sciences have shaped institutions, procedures, instruments, spaces of operation, and forms of capitalization. This logic facilitates a mercantile approach to life, where safety is commodified.

The role of decontextualization in aiding imagination and resulting in novel artificial artefacts is exemplified by the development of the revolutionary technique PCR (Polymerase chain reaction).<sup>85</sup> In Paul Rabinow's (1996) book *Making PCR: A Story of Biotechnology*, he explains that for Kary Mullis (the inventor of the technique), the components that constitute PCR had been available for some years, like synthetic nucleotides and polymerases. What was a breakthrough, was the concept, the idea of putting them together into an assembly to synthesize DNA fragments. As Rabinow explains, for Kary Mullis what was remarkable about PCR (as a concept) was the idea to take DNA out of its context.

One of the few commentators that have studied xenobiology, Bernadette Bensaude Vincent (2013b), makes a similar critique to synthetic biology and xenobiology. She is concerned with the ontological status of xenobiological objects, and how advances in the field that aim to 'emancipate' humanity from nature leads to undervaluing of living beings. A consequence of molecularization is that novel artefacts or biological systems are constructed, and the experimentation—design process can be successful without needing to consider interactions with the wider world, or the 'milieu' that such artificial organisms can inhabit (more in **Chapter seven**). Bensaude Vincent writes (p. 374), referring to the 'objects designed' in xenobiology:

Like soil-less cultures they are designed to operate off-ground, *independently from the cell's natural environment. They are deprived of autonomy, and of the mobility and capacity to enter into new associations with their "milieu."* As products of human design, they are neither the outcomes of contingent history like living beings, nor the outcomes of a process of individuation as concrete technical objects. They ignore the interdependency of individuals with their environment as well as the interdependency of present, past, and future, which characterize the mode of existence of natural and technical objects (emphasis added).

Then she connects these concerns with safety-by-design, and writes:

As long as containment is the major concern of synthetic biologists, the problem of coexistence and synergies between synthetic organisms and natural organisms, which have acquired evolutionary capacities through billions of years, cannot be addressed. Therefore, such biosynthetic objects share no community of interests with living beings. There is no way for them to participate in a common world. They are from nowhere, from no time.

Along with the role of time in xenobiology, her perspective raises issues of the instrumental use of genetically modified organisms. These organisms, or objects, lack a common evolutionary history with all living beings. In the minds of xenobiologists this is not a problem, because xenobiology is about expanding the boundaries of life to include forms of life that were not selected through evolution. As Bensaude Vincent focuses on time, for me it is relevant to consider the *origin* of xenobiological objects, how they come into

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<sup>85</sup> Widely used technique used in molecular biology to exponentially amplify a single copy or a few copies of a specific segment of DNA to generate thousands to millions of copies of a particular DNA sequence. See Kary B. Mullis' Nobel Lecture – 'The Polymerase Chain Reaction', <https://www.nobelprize.org/prizes/chemistry/1993/mullis/lecture/> (last visited September 30, 2018).

existence. As she claims that xenobiological objects “are from nowhere, from no time,”<sup>86</sup> xenobiology adds a degree of heterogeneity to the repertoire of living organisms without precedents. XNA-based forms of life might not have a lineage, but their incorporation into the world certainly will raise challenges and opportunities.

Returning to the main argument of this chapter about redefining and rethinking life, in xenobiology, the barriers of thinking about what is possible are erased. In principle, anything would be possible; any enzyme could be created, as long as there are sound methods to ‘find it’ or ‘doing it.’ Research in xenobiology depends on the premise that it enables imagining life in new ways, as life becomes an exercise of reshuffling existing components and creating new ones, which although often are analogues of existing natural components (like DNA or polymerases), they are considered ‘never born,’ or ‘new to nature.’ Creating novel components is possible through directed evolution because interventions are being made at the level of the molecule, the enzyme, not the cell.

#### 4.4 Exploring limits

Expanding the possibilities of life by developing unnatural organisms can be perceived as controversial or transgressive. In what follows, I elaborate further on the sociotechnical imaginary of ‘life unbound’ in xenobiology, related to the work needed to maintain the discipline as a legitimate and acceptable enterprise. Part of the work requires positioning xenobiology as a safer option than its natural counterparts (i.e., Marlière, 2009). Seeking legitimization can be interpreted as a way for xenobiologists to occupy niches that other areas in the life sciences cannot fill, by promising narratives of safety that are not accomplishable by other means. A niche space is created by the notion that the unnatural is the safest option, facilitating and justifying the release of genetically modified microorganisms in open environments.

The language used to refer to the exploration of limits may seem inflammatory, as one interviewee manifested. But it serves to appeal and capture the imagination of scientists in a regime in in a field where competition for resources and attention is fierce. The limits and metaphors I present below draw upon an imaginary of life unbound and cultural resources of molecular biology that I have already described. Narratives like ‘the farther, the safer’ are mainly the result of the work conducted by Philippe Marlière, Victor de Lorenzo, and Markus Schmidt, vanguards of xenobiology (Hilgartner, 2015). As such, they matter insofar

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<sup>86</sup> Biotechnological artefacts are brought into being thanks to the power of directed evolution techniques,) which can be interpreted as a multitude of evolutionary events, compressed in time, manageable by a laboratory practitioner. For me it is puzzling where objects or ‘tools’ –like enzymes and polymerases that replicate XNA– come from.

they recruit collective ideas, assumptions and symbols about biotechnology and xenobiology which are important to understand how a rhetoric of safety and responsibility is constructed and expected to fulfil its instrumental role of earning public trust and resources for research.

#### 4.4.1 Navigation & distance

In **Chapter one** I explained that xenobiology has been associated with ideas and visions of ‘exploration’ by the French synthetic biologist and entrepreneur, Phillippe Marlière, who organized the first xenobiology conference.<sup>87</sup> In the ‘synopsis’ section of the conference website it reads “The venue for the XB1 conference was chosen in the hope that Genoa’s illustrious citizen Christopher Columbus will *inspire the exploration of yet unknown continents of life*” (emphasis added).<sup>88</sup> This hints at the aspiration of the field to redraw the boundaries of what is understood as life, using the metaphor of navigation. But what type of space is being navigated, and in what terms? The non-profit Austrian organization *Biofaction* prepared a short video clip<sup>89</sup> about the conference in which Philippe Marlière appears in a background with classical music, in front of a replica of a beautiful galleon stationed in the port of Genoa; after various close-ups to the ship, Marlière states:

Biologists now are like navigators in the Renaissance, because we don’t know enough, but we can move away from the natural world, and try to reach virtual continents of life, so to speak, so Christopher Columbus, appears as the icon for organizing this first xenobiology conference. And where was Columbus born? He was born in Genoa. That’s where we are.

These opening remarks by one of xenobiology’s main spokespersons attests to the importance of navigation and exploration for the nascent field of xenobiology. The concept of navigation was transversal to the conference, as shown in *Biofaction*’s video where a wooden model of a galleon sits on top of a table of panellists (**Figure 4**). Navigation involves exploring territory that is not known beforehand, and it applies to biology, in the sense of exploring novel forms of life that cannot be determined in advance. The systems or forma XNA-based organisms will adopt can only be discovered as advances are made in the field.

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<sup>87</sup> See footnote 5.

<sup>88</sup> Ibid.

<sup>89</sup> Ibid.



Figure 4. Panel in the first Xenobiology Conference. Note the presence of a Galleon, to remind the audience that xenobiology is a field for navigators. Snapshot of videoclip available in <http://xb1genoa.com/>

Xenobiologists are portrayed as not merely scientists, but *navigators*, eager to take on grandiose challenges. Marlière often speaks of ‘virtual continents of life’, creating both a unique, unoccupied space, and a sense of distance. Although such a biological space is created through genetic engineering or molecular biology, but what constitutes it is far from clear. Conducting xenobiology both through metaphors and in the laboratory implies the creation of such a space. In a talk titled ‘*Accept No Limits*,’<sup>90</sup> during a conference on cellular and molecular biotechnology, held in the *Institut des Hautes Études Scientifiques* (IHÉS) in Paris in December 2015, Marlière refers to his development of a microorganism (*E. coli*) that was evolved to depend on the nucleic acid Chlorouracil, a DNA analogue.<sup>91</sup> He framed this endeavour as the “exploration of xeno-DNA,” adding, “This is about navigation. This is a metaphor that we use with the public, but we find it pretty accurate.” This suggests an ‘emancipation’ of mankind from the pressures of nature, which has also been used by Marlière as a need to emancipate from the limited array of solutions to be found in the research of life based on DNA.

The discourse surrounding ‘exploration’ reflects a particular way of understanding the limits or boundaries of life. For Marlière, life is not about organisms based on DNA, but organisms that can *proliferate*, or ‘replicate chemically.’ His discourse is based on a different understanding of life. If all forms of life that could proliferate have the same ontological status, that is, could have existed, then it is possible to speak of ‘life as we don’t know it.’ In his words,

<sup>90</sup> See footnote 63.

<sup>91</sup> See Marlière et al., 2011; explained in **Chapter one**.



Xenobiology is about living organisms, chemically deviant from terrestrial life as we know it, whether it is extra-terrestrial or made here, using genetic techniques, or organic chemistry techniques and so on. Just a very simple metaphor, as I said, is to consider possible... if we ask ourselves... what is able to proliferate, to replicate chemically?

This shifts the centre of life from the molecule that allows heredity, DNA, to processes of replication and propagation of information. However, the use of the navigation metaphor goes beyond employing a different understanding of life. Marlière draws on a cultural resource of biology, related to evolutionary biology, as noted above. In his talk, he refers to a '*chemical space of life*' that in principle could function with any organic molecule (having as a condition, that the resulting organism or system would proliferate). He relates this space to "John Maynard Smith, who described the evolution of organisms as trajectories in the combinatorial space of sequences of ATGC." In 1970 Maynard Smith wrote in response to a discussion over the possibility of natural selection to explain the rise of functional proteins: "Suppose that we imagine all possible amino-acid sequences to be arranged in a "protein space," so that two sequences are neighbours if one can be converted into another by a single amino-acid substitution" (Maynard Smith, 1970: 564). Briefly put, the debate addresses how functional proteins came into existence among a vast amount of protein sequences (in the protein space) that are not functional. Hence, how can functional proteins be selected? For our purposes, what matters is the mobilization of concepts from (molecular) evolutionary biology<sup>92</sup> to give context to a discipline that aims to reconfigure known genetic systems.

The 'protein space' (**Figure 5**), understood as a set of possible proteins, raises the question of how much of it has been 'explored' by life on Earth (Dryden et al., 2008). In connection to the dichotomy between the natural and the synthetic, for biologists, the natural proteins are the product of the historical evolution of life on Earth. If there are proteins that are not present on Earth, it is because they have not been explored, and are what biologists call '*never born proteins*' (cf. Chiarabelli & De Luca, 2007; Luisi, 2006). The fact that a large proportion of proteins have not been explored or have not been selected through the vagaries of evolutionary processes, does not mean that they should not exist, but rather, they have not been explored. These moves represent a shift in thinking from organisms and molecules to life as information storage (and propagation). As interviewee 5C expressed, "I can give you the most fundamental system in life is information storage. And if we can go in and create a new base pair, that suggests that there's nothing fundamentally different from G, C, A, T, because we can go in and create X and Y." Thinking of life as information that propagates itself is useful for xenobiologists as they focus on the imagination of forms of life not known yet, without considering the evolutionary history of all living organisms.

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<sup>92</sup> The idea of a 'landscape', as a space that living organisms constitute, can be traced back to the idea of a 'fitness landscape', first suggested by Sewall Wright in 1932. See Provine, 1986; Wright, 1932.

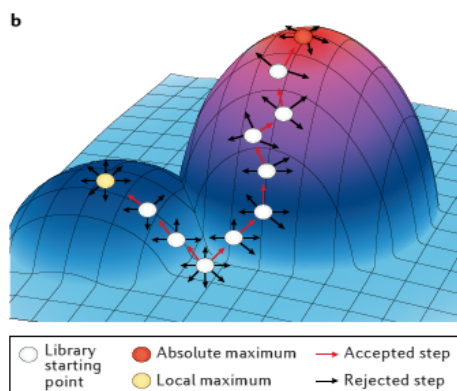


Figure 5. Visual representation of the 'protein space', in terms of directed evolution, in which a protein moves along the protein space, from one point (a hill) to another with a higher fitness. Source: Packer & Liu, 2015: 380.

This facilitates the imagination of alternative biological worlds within a biological (sequence) space that in theory is not bound by any limits. Placing natural organisms at the same sequence space as synthetic organisms also plays a function of eliminating distinctions between them, helping to ignore the fact that natural organisms are the product of a unique evolutionary history. The question for the scientists then becomes how to reincorporate the materiality of the sequence space, or rather, how to turn the multiple possibilities of different proteins or organisms into actual organisms with a physical presence in the world. In other words, how to engineer organisms based on an *imagined sequence space*. The laboratory becomes a place where distances (in an imagined sequence space) are made non-existent and turned into challenges that are tackled through tools of organic chemistry and molecular biology. As distances become easier to navigate, or to cross, 'new biological worlds' become less alien to us and more familiar to us.

During the XB1 conference, other pioneers of xenobiology who participated in the conference did not refer to xenobiology as being a scientific field of *navigation*, and instead talked about the rationale behind this, relating xenobiology to exploring the biological space, was present. For instance, in the Biofaction' video, Phil Holliger states: "Evolution is a tinkerer. It tends to build on what has come before and tried to fix it. So, it's not something that is, you know, works by design, but rather by, you know, keep adding to existing structures and modifying them step by step." In a similar vein, summarizing the discussion above, Rupert Mutzel, a German synthetic biologist, who also appears in the Biofaction video, explained that there are many forms of life that could be brought into existence, but some possibilities have not even been given a chance: "It's like in technology. It's like in daily life. You can be very reluctant to changing that. Most biologists would tell you that nature has tried everything that was possible. But it turns out that it's probably not the case." This quote captures the rationale behind searching for limits in xenobiology: there is a limit in terms of what nature has tried out during evolution, due to evolutionary constraints and

not because it was not possible in the first place. Navigation is about charting evolutionary distances.

At the beginning of my fieldwork I attended a presentation by the principal investigator of the laboratory, titled '*Synthetic Biology through Directed Evolution*,' in which he provided a vision for the laboratory. For the researchers involved in synthetic biology, it is useful to think of the 'sequence space,' and for some projects, ask the question: how to move along (or navigate) the sequence space in order to create tools (i.e., enzymes) to manipulate XNA-related components. It is telling that one of the papers presented in the laboratory meetings, titled *Environmental changes bridge evolutionary valleys*,<sup>93</sup> addressed the subject of navigation and directed evolution in depth. In the article's abstract, the authors state "In the basic fitness landscape metaphor for molecular evolution, evolutionary pathways are presumed to follow uphill steps of increasing fitness. *How evolution can cross fitness valleys* is an open question" (Emphasis added). In the article the author explained that the lessons were derived for selection techniques based on directed evolution, highlighting the claim that negative selection is viable to select mutants that otherwise would lie outside local optima, using a 'tuneable selection system.' The use of space is used to conceptualize techniques that are put into practice in the laboratory. It is not a far step to think of crossing fitness valleys, as the quote above, in terms of new biological worlds. Then, xenobiology, as a way of thinking and handling materials related to life (or the biological), should be understood in terms of how the realization of directed evolution experiments relies on an imagined sequence space.

I am not aware that the metaphor of navigation has caught on or become a collective signature of xenobiology. The metaphor of navigation that Marlière and Schmidt propose does not seem to be 'mainstream' among xenobiologists or synthetic biologists. The association of metaphor with evolutionary biology was evident in the scope of the laboratory I studied. In the laboratory, there was no reference to visions of navigation or exploring what is not known to nature, and even in the laboratory discussions, when I made references to these metaphors, there were researchers that were not familiar with them. The laboratory I studied aimed to position itself as a 'one stop shop' for directed evolution, as the principal investigator once explained to me, in the sense of building tools and methods that others can use and apply toward the solution of a wide range of problems.

In the laboratory, the metaphor of navigation acquired a different meaning. As suggested by the principal investigator of the laboratory I studied, navigation could be interpreted as walking in the 'fog' without knowing what steps are doable, or where a project will take them. It is possible to get lost and difficult to return to a desired course. Therefore, there is

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<sup>93</sup> See Steinberg & Ostermeier, 2016.

distance between having a vision and a local path to open or cross through. The strategy of the laboratory is then to take small steps, within what remains visible, making a map of a larger scale while the projects advance. That difficulty of making decisions on a day-to-day basis, without much certainty of whether results are achievable, makes it difficult to think about the ‘big picture’ of research, at least for doctoral students and post-doctoral researchers, who have another preoccupation –securing a job.

As Marlière puts it, navigation encloses more than moving among the ‘protein space’, or ‘the chemical space of life.’ It is about the difficulties and the process involved in using directed evolution (what he calls Darwinian evolution) as a method to create, or encounter, those forms of life not known to the world. That is, using navigation not only as a metaphor to describe that life is made of both the organisms that were, and the organisms that could be, but in practice it refers to how researchers think about the experiments they carry out to advance the aims of xenobiology. Marlière summarizes this relation between the practice of xenobiology and the notion of life, by saying, “Xenobiology, in the same sense, it’s an exploration that is not reducible to biology as we understand biology. It’s not just a matter of giving an account of life. It is how to explore other forms of life.” The metaphor of navigation and exploration has performative power: it channels resources and attention of the scientific and policy communities towards particular commitments about trajectories in the life sciences. As explained above, Marlière associates navigation of ‘new biological worlds’ with providing safe-by-design organisms, what he refers to as “the farther, the safer” (Marlière, 2009). This is a crucial move, since exploration is not usually authorized merely for the sake of exploration or discovery. Conversely, it is usually tied to rewards and benefits, as the social contract for science suggests (cf. Wilsdon, Wynne, & Stilgoe, 2005).

#### 4.4.2 ‘The farther, the safer’: a safe space for experimentation

The metaphor of navigation is appealing as a cultural inspiration. A case in point is provided by Craig Venter’s bio-prospecting expedition in 2003 to sample the genomic diversity of marine micro-organisms. His team’s voyage followed the routes of two of the great scientific explorations of the nineteenth century, the voyage of Charles Darwin’s *Beagle* and that of the British oceanographic vessel *HMS Challenger*. Venter’s expedition was tied to a sense of appropriation of the biological, constructing subjects and objects of ownership (Pottage, 2006). However, for Marlière (2009), navigation implies going far away or the ‘*the farther, the safer*.’ His notion of navigation is tied to safety: the risks of the field lie in exploring the ‘coasts,’ or nearby borders of biology. In other words, the risk lies in organisms that bear similarities with DNA-based organisms. Marlière writes:

The word “cabotage” was coined by Spanish seamen to describe the safe navigation from cape to cape, in contrast to perilously sailing away toward open seas. Metaphorically, it is by restricting itself to exploring the vicinity of the known continent of life and staying near the shores and capes, the latter perhaps represented by extremophilic organisms, that biotechnology keeps steering evolutionary trajectories that do not depart from known forms of life (Marlière, 2009: 79).

The risks are framed as staying near the shores and capes, which represent the known biological world. Remarking that serious hazards come from DNA-based organisms (like pathogens), Marlière states: “the surest if not simplest way to avoid risks of dissemination and contamination by potentially harmful synthetic species will be to evolve chemical constitutions *as deviant as possible from that of natural species*, and to rely on the persistence of these constitutions as a built-in measure for counteracting the colonization of wild habitats, including the human body” (ibid., p. 80; emphasis added). The idea that risks are higher for ‘natural organisms’ than synthetic ones is a common view in synthetic biology, but only spokespeople like Marlière push metaphors of navigation that capture the message so boldly. Without referring to metaphors of navigation, Japanese chemist Ichiro Hirao also suggests that departing from nature can constitute safer (contained) genetically modified organisms. For example, he states:

The next goal is to apply unnatural base pairs to in vivo systems, by which the present genetic recombination techniques would be changed to a new genetic expansion technology. *This new technology could provide safer containment technology than the present recombination technology*. Since unnatural base pairs cannot be synthesized in a metabolic pathway, their nucleoside materials must be supplied as a nutrient from the outside, to maintain the artificial genes containing the unnatural base pairs in the cell. Thus, a cell lacking the nutrient cannot live (emphasis added) (Hirao & Kimoto, 2012: 361-362).

However, the message of navigation and exploration of uncharted territory is inherently a discourse of domination of man over nature. Stories of exploration have consisted of conquest, exploitation, suffering, and pillage. Europeans and non-Indigenous, non-Black Americans have traditionally thought they could do whatever they wanted in an environment that is new to them. Implicit in the message of navigation is that (expanded) life can be exploited. Thinking of life as what is biologically possible serves to strengthen this claim, since scientists then become limited only by what is possible, and by what society is willing to accept. In the metaphor of navigation, its symbolic and cultural baggage seems to be lost along the way. It negates the value of the ‘other,’ of shores or lands that are found, to become the property of whoever claims them. Exploration also ignores that xenobiologists do not encounter ‘life as we don’t know it,’<sup>94</sup> but they actively construct the forms of life they claim to find. Furthermore, the metaphor of navigation has attached components of colonization and domination, that extend to different spheres of societies around the world as a main cause of global inequalities. Xenobiology also seems to capitalize on a narrative of Western success through science and navigation, which is becoming more and more disputed

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<sup>94</sup> See footnote 8.

as time moves forward. My point is not that using metaphors of navigation in xenobiology is illegitimate, but that by doing so, researchers open a door for cultural meanings that merits reflection and engagement with historical and political events.

In essence, navigation encompasses a distinction between a DNA-based world and an XNA-based world. Recurrent in debates in biosecurity in synthetic biology, hazards are associated with DNA-based organisms.<sup>95</sup> For instance, synthetic biologist 5C commented in an interview: “Nature doesn't need any help being nasty. Take a look at smallpox, the virus. Take a look at the Black Death in Europe. There's nothing that we're going to do that is going to make nature more nasty.” The association of departing from nature as a safe enterprise has been suggested by synthetic biologists like Víctor de Lorenzo (2010), who classified a spectrum of a “transition between naturally-occurring organisms and wholly synthetic microbes” (**Figure 6**). He makes a similar claim to Marlière's ‘the farther the safer,’ or as he writes, “It is sensible to propose that the more synthetic microbes are, the less risky they also become” (ibid., p. 929). In addition, de Lorenzo claims that risks are presented by pathogens. He even suggests that synthetic organisms (the farther) may contain unexpected properties which may make them risky, hence providing a rationale for their containment. If risk becomes a measure of naturalness, other considerations about values and visions of natural and social order can lose importance or priority in an agenda about ethics and social ramifications of xenobiology. Schmidt and de Lorenzo (2012) make a connection between safety, (un)naturalness, and release, which is essential for constructing the space that only xenobiology can occupy, of being both safe and synthetic. They write, “There has been little evidence for any serious mishap that could be directly linked to the accidental or intentional release of engineered microorganisms. In the meantime, a large number of incidents involving natural pathogenic bacteria and viruses have indeed happened” (ibid., p. 2199).

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<sup>95</sup> This owes to the interconnection between pathogens and hosts, which has been forged during thousands of years.

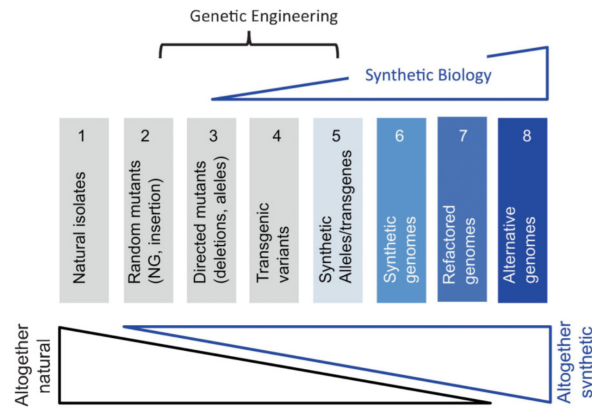


Figure 6. Classification of a spectrum of overlapping between natural organisms, genetic engineering, and synthetic biology<sup>96</sup>. (de Lorenzo 2010: 927).

Markus Schmidt (2010) suggests that xenobiology is inherently safe because organisms would not transmit genetic material and their growth could be controlled. Framing xenobiology as a safer option to DNA-based biotechnology is strengthened by the notion of a ‘safe space for experimentation,’ as Schmidt suggests (see **Figure 7**). The terms under which experimentation could take place in such spaces are not defined, and rather imply that thresholds, regulations and limits would not apply as usual. This seems as an ideal Baconian space where research can be conducted free of moral obligations. The arrangement of a space restricted for the laboratory, in which consequences of scientific research should not reach society, is extended to xeno-organisms, by virtue of their built-in isolation from nature. In Schmidt’s logic, and interpreting the figure he included in his article (**Figure 7**), different genetic constitutions based on DNA or XNA can remain isolated from each other, effectively creating separate worlds. Schmidt writes, accompanying the caption of the figure, “[n]on-DNA-based biological systems will be a safer place to conduct SB [synthetic biology] experiments and applications” (ibid, p. 327). This is used to argue that the uncertainties of xenobiology can be effectively managed.

Schmidt does not elaborate in depth the notion of xenobiology as a *space for experimentation*, and neither do other researchers in their articles or the conversations we had<sup>97</sup>. Connecting navigation to the plasticity of life, in the *Biofaction* video of the XB1 conference<sup>98</sup> Marlière further states, referring to xenobiology, “It is a matter of having

<sup>96</sup> In this classification, only the category number 8, ‘alternative genomes’, corresponds to xenobiology.

<sup>97</sup> An interesting point has to do with the use of xenobiology in DIYbio movement, or hackspaces. The literature on the subject does not cover the topic, but in a conversation with the PI of the lab I studied, I asked him if he saw DIYbio as an opportunity for using xenobiology. He replied that this was not among his priorities, and there were several strains that were already impaired which DIYbio enthusiasts could work with.

<sup>98</sup> See footnote 5.

alternatives and growing other trees of life. And in a way, it is a discipline for modest creators.” Life is understood as an evolutionary process, but not a unique one.

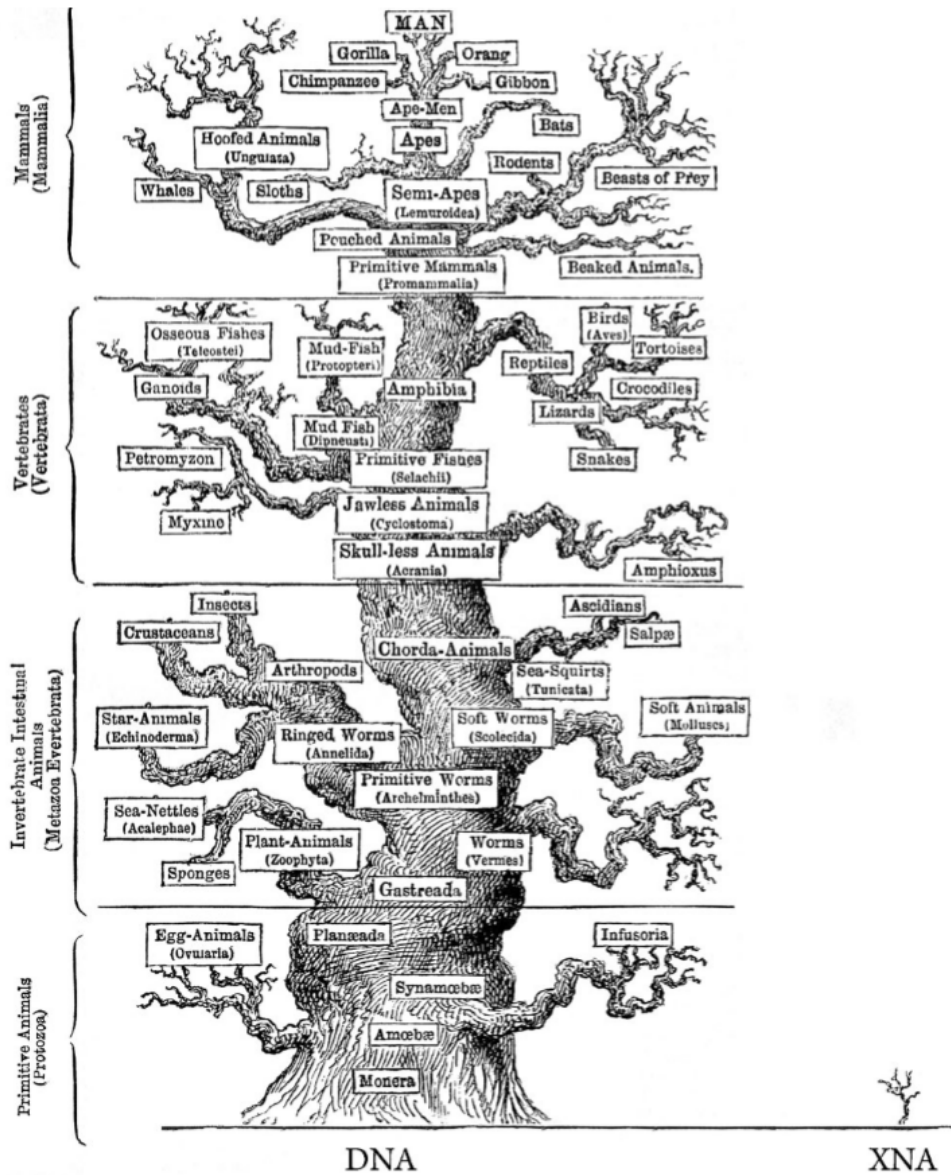


Figure 7. Xenobiology can provide a second tree of life, as a safe space for experimentation. See Schmidt (2010: 327); Schmidt acknowledges that the tree of life displayed is a modification of Haeckel, 1883.

In Schmidt’s depiction of a ‘safe space’ for experimentation the notion of space is based around a notion of space and distance as evolutionary, or genetic. The creation of safe spaces for research is a feature of a regime of ‘technoscientific promises’ (Stilgoe, 2016: 864), which favours practices of purification (Latour, 1993). In Schmidt’s tree, the distance that separates XNA-based organisms and DNA-based organisms is imaginary, an abstraction or fiction. Although the two trees appear separate and far from each other, in practice there is no such space in which the two can coexist isolated. They might not be capable of transferring genetic information, but they would occupy the real world, as they are inevitably entangled.



Noteworthy, advances in xenobiology so far that aim to develop organisms that incorporate XNAs *in vivo* are fully dependent on DNA as well.<sup>99</sup>

Discourses and metaphors are useful to talk about and describe processes and operation previously not known, or not fully understood (Keller, 2002); as such, are performative and have power to shape actions and policy responses. Hence, treating XNA-based life as a second tree of life represents a way of thinking about experimentation in the natural sciences and dealing with risks and hazards. Although Schmidt's tree appears humble and tiny in comparison to the DNA-based tree of life, it captures the imagination of scientists in powerful ways; it invites people to think of XNA-based life as inoffensive and controllable. It reduces the seriousness of modifying the boundaries of life. If the tree of life works as a visual aid to think about evolution when two different trees are juxtaposed in the same 'space', the result is obliterating differences between organisms and species; it silences their stories and justifies mixing them and entangling them. The same space suggests that both trees are subject to the same type of rules. However, the depiction of 'trees of life' aims to make genealogies and evolutionary histories insignificant, helping to maintain distinctions between domains of life (i.e., DNA and XNA trees) because this helps to reinforce that the more unnatural, the safer, a niche that only xenobiology can occupy. Franklin (2000) argues that the Darwinian model of life is based on vertical, genealogical descent. Life is lineal, connected by descent; its orientation is forward, cannot go back in time or in generations. For her, cloning and genetic engineering disrupt these restrictions on heredity, what Franklin calls the 'respatialisation of genealogy.' Genealogy and pedigree are no longer significant, and 'genealogical time is as irrelevant as species borders' (ibid., p. 219). According to Adrian Mackenzie (2010: 195), "Synthetic biology also imagines a hyper-flattened terrain of inter-species difference, the design processes taking shape there in some ways twist and subduct that flatness." Such disruptions of meaning when inheritance is referred to is an important locus of analysis.

I did not find further references to xenobiology as a 'safe space' for experimentation in my fieldwork, which suggests this is not a commonly held view. Nevertheless, judging the tone of the presentations about synthetic biology and xenobiology that I observed, for example the development of platforms to conduct 'rapid evolution' without interfering with existing biological processes,<sup>100</sup> what best encapsulates the idea behind 'safe spaces' is the ability to explore the multiple possibilities of life without interfering with DNA-based life.

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<sup>99</sup> For example, the semi-synthetic organisms that Romesberg lab has developed over the past years function with alternative nucleic acids as an addition to an existing cellular machinery that works with DNA (cf. Malyshev et al., 2014; Zhang et al., 2017).

<sup>100</sup> For example, the laboratory of Chang Liu in the University of California Irvine. See <https://liulab.com> [last visited July 24, 2018].

This supposes a move to expand the possibilities of life rather than establish boundaries between DNA-based life and life supported by different genetic systems. In my interpretation, this derives from an imaginary according to which life can be safely played and experimented with, without altering the balance of existing organisms and ecosystems. I return to the consequence of thinking about demarcated spaces in xenobiology in **Chapter seven**, in which I raise questions about the potential ecological impact of xeno-organisms.

#### 4.4.3 Limits and responsibility

Thinking about life as a space in which multiple forms of life can coexist is part of the identity of xenobiology, and navigation as stepping into unknown biological worlds and testing limits, brings along questions of policing and responsibility. Policing involves more than monitoring or assessing the side effects of experimentation in xenobiology, but reflecting on what issues may be overlooked, exploring the limits of our knowledge. What authority do scientists have to explore life at its limits? Who gets to decide when they have gone too far? This question is taken up by George Church in 2007, who commented in an interview for the portal/website *Edge* with Seth Lloyd (Professor at MIT),<sup>101</sup>

Many of the people here worry about what life is, but maybe in a slightly more general way, not just ribosomes, but inorganic life. Would we know it if we saw it? It's important as we go and discover other worlds, as we start creating more complicated robots, and so forth, to know, *where do we draw the line?* (emphasis added).

Later in the conversation, Church provides an answer, referring to research being limited by the possibility of facing risks:

What we're trying to get at when we're doing synthetic biology; we're trying to increase diversity, increase replicated complexity, and maintain our ability to continue to do that for many years, and we don't want to endanger that by doing something that's too risky.

Thinking of limits as a line not to cross, or a threshold, diminishes the quality of conversations around xenobiology that society (including the scientific community) should engage with; nevertheless, establishing thresholds or limits is complicated, and potentially may lead to controversies (Stilgoe, Watson, & Kuo, 2013). Whether crossing a boundary between the natural and the unnatural is considered hazardous is tied to the visions and imaginaries of xenobiology that broaden our understanding of life. If we think of life as plural, being constituted by multiple possibilities, then navigating possibilities that did not arise through evolution seems like an innocent idea.

Nevertheless, speaking of limits and moving across spaces or distances is tied to questions about *control*. For instance, advances in biomedicine represent an age of 'biological control.'

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<sup>101</sup> Retrieved from [https://www.edge.org/conversation/george\\_church-george-church—life-what-a-concept](https://www.edge.org/conversation/george_church-george-church—life-what-a-concept) [last visited September 10, 2018].

Sarah Franklin draws upon Ian Wilmut, one of the cloners of Dolly the sheep, to write: “This means that we can no longer assume that the biological ‘itself’ will impose limits on human ambitions. As a result, humans must accept much greater responsibility toward the realm of the biological, which has, in a sense, become a wholly contingent condition” (Franklin, 2003: 100; cited in Rose, 2006: 16). Embracing responsibility involves more openness and deliberation about the prospects of a field as xenobiology. Hence the importance of exploring what is understood as ‘control’ in the life sciences, especially when control over nature, by experimenting with what is possible, can be confounded with exerting responsibility. Limits are tied to control and responsibility because they underlie a capacity of scientists to detect limits, impose them, and crossing them. Pioneers of xenobiology seem to be concerned with addressing responsibility from an early stage, but this converges with developing built-in safety features, leading to the discourse required to frame xenobiology as an expansion of biology, as a space to be reached which is safer to experiment with than the natural world. This prompts to ask, under what terms is it legitimate to explore the boundaries of life? What is allowed and what is to be gained? A relevant consideration is whether xenobiology—and more broadly safety-by-design— can provide an illusion of control that may backfire.

Much of xenobiology’s scientific practice relates to what we do not know. As an exploration, a navigation of new biological worlds, researchers do not know exactly where they will arrive. They do have (design) guidelines of what an XNA-based world should behave, but it is based on imagination and speculation. Researchers support the thinking that life is in constant motion, always evolving, without being definite. We do not know how life came into play, or whether it has limits, or where life begins and ends. Dealing with such uncertainties (**Chapter seven**) is important when providing an account of responsibility and control when expanding or shifting limits. Some researchers in xenobiology seem to be aware of the complexities of experimenting with the life at its limits. Torres and colleagues (2016) wrote,

Lack of specific knowledge is not an impediment if pre-emptive action can be taken to address the sources of potential risk. For instance, *although we may not be able to foresee how every GMO can interact with the environment and how likely those scenarios are, we can still tackle its potential sources of risk to the environment*, i.e. GMOs interacting with the environment as organisms or the information coded by the GMO (e.g. antibiotic resistance) being passed onto the environment (ibid., p. 393-394) (emphasis added).

This way of thinking reflects awareness about non-knowledge, but at the same time assumes a position from which potential risks and sources of controversy can be known, rather than displaying a disposition for learning. Despite this limitation, recognizing what we cannot foresee is a good starting point, paving the way for anticipatory approaches of governance (Barben et al., 2008). Torres and colleagues (2016) elaborate further on the subject, suggesting that containment can be used to prevent identified hazards. They add,

Containment naturally emerges from that framework and its goals are clear: avoid, prevent and minimize –avoid known traits that are likely to benefit GMOs in the natural environment, prevent GMOs from entering the environment and minimize any potential penetration into the environment. The same criteria are also applicable to any genetic information used in engineering an organism since exchange and acquisition of genetic information, better known as horizontal gene transfer, particularly for microorganisms, is common in the environment (*ibid.*, p. 394).

The authors do not necessarily imply that containment can prevent all hazards presented by genetic engineering, but it is an opportunity to interrogate the imaginaries and visions that drive the emergence of xenobiology, since in framing what is controllable, what is known, and what is possible, we can find an important locus of power in establishing this emerging field. Manipulating life to the point of determining what is biologically possible and when imagination meets reality, runs the peril of being hubristic. Not only in terms of experiments that can go wrong and controversies that may arise, but also in changes of how we relate to life and value it.

In summary, the question is whether we can trust scientists to know what limits not to cross, and to identify what should not be done (in agreement with society's values and appreciation of nature). In creating a safe space for experimentation, there may not be accountability, because it is scientists who make the rules and occupy the space. Expanding limits encompasses more than tracing divisions between the inside and the outside, between the DNA-based world and the XNA-based world, between life with a genealogy as opposed to 'flattened' life involving caring about them and having good reasons to experiment with them or getting near to the borders, where the unexpected is normal. If life is viewed as what is biologically possible, then it is in the hands of scientists to tell what is worthy of life. But it is not up to them to determine how far to experiment within the (expanding) boundaries of life. Responsibility could be reduced to ensuring that safeguards are in place. I continue developing ideas on responsibility in xenobiology in the coming chapters.

#### **4.5 Summary and conclusions**

The above discussion has sought to gather elements of a sociotechnical imaginary of 'life unbound', according to which life is malleable to the extent that it is biologically possible. Life in this sense is not restricted to an evolutionary history, but what can be accomplished in the laboratory. In this chapter I have proposed that xenobiology is best understood as a way of thinking about life, as being unlimited. I have shown the cultural resources from biology that enable rethinking the foundations of biology. I also examine the rhetoric that the unnatural is the safer option. I encapsulate these ideas under the sociotechnical imaginary of 'life unbound.' In this chapter I have referred to limits as constraints of what is achievable in biology, and boundaries as to what we understand as the main features of living organisms

–functioning on a universal genetic code? Having a genetic system that works on DNA? Having evolved from a ‘last universal common ancestor’ (LUCA)? For synthetic biologists, especially those involved in advancing xenobiology, that “biology is not limited by what is natural, but rather, by what is possible” (Torres et al., 2016: 395).

For the lay person, exploring the limits of life (as I propose that xenobiologists do) may seem transgressive. In this thesis, I point out that such transgressiveness and potential to stir controversy is possible by virtue of transforming norms and conventions about what research about life is socially permitted. Hence, xenobiologists require to legitimize experimentation in their field. Testing what is biologically possible needs to be acceptable by society. My analysis of the rhetoric that the field’s pioneers mobilize to gain legitimacy suggests that xenobiologists draw on (and challenge) existing cultural resources in the life sciences, such as DNA not being the ‘molecule of life,’ that biological systems can be disaggregated or molecularized, and that there is still no biology in xenobiology. These may not be deliberate tactics to earn the legitimation of xenobiology but serve to understand how scientists think about (and redefine) life, which is useful to understand the dynamics between scientists and society.

In the second part of this chapter I address the narrative of xenobiologists as explorers of new biological worlds, navigating the uncharted territories of life beyond DNA. This has been mainly proposed by Philippe Marlière and Markus Schmidt. Such metaphors of navigation are based on concepts from evolutionary biology. Even though Marlière has been labelled by an interviewee as ‘inflammatory,’ such eccentric depictions of research in xenobiology are necessary to draw attention to the field, resulting in the recruit of researchers and funding. I did not find ample support for these ideas; as such, they can be understood as a form of sociotechnical vanguard (Hilgartner, 2015) that have not yet achieved a collective character. Nevertheless, I draw attention to the building blocks that enable them: cultural resources of evolutionary biology.

The exploration of new biological worlds, or as Marlière has expressed, ‘accepting no limits,’ involves redefining life and decoupling its identity from DNA. Are xenobiologists expanding limits or creating new territories of life? I suggest that xenobiologists seek both avenues. Life based on XNA and alternative genetic systems aims to avoid being treated as unnatural. Limits can be crossed only if they are thought to be safe, at their borders and beyond. If life is redefined as elastic, as mechanistic rather than contingent on historical (evolutionary processes), then the limits of xenobiology expand life. At the same time, proponents of the field like Markus Schmidt seek to create “safe spaces for experimentation” (cf. Rip, 2011), as xeno–organisms would constitute a tree of life different from DNA–based life.

Concern over limits raises a number of questions about responsibility. Exploring life at its limits involves researchers establishing how far they should go, and to what extent what they do is admissible. Researchers create a niche that only they can occupy, in which xenobiology can fulfil a promise of safety by design in biotechnology. Thinking of spaces of experimentation puts into question who gets to participate in decision-making, and who polices life at the limits. It runs the risk of becoming an ungoverned territory, if we place too much confidence in governance by containment, and an illusion that control in biological systems is feasible.

In the next chapter, I suggest that governance by containment, and the association of xenobiology with safety both obey a sociotechnical imaginary of ‘controllable emergence,’ according to which governance matters can be addressed by design principles (i.e., biocontainment) and that ensuring control over life can ensure the respective control of public acceptance.

## 5. Biocontainment as built-in governance

### 5.1 Introduction

In this chapter I analyse xenobiology and its promise of biocontainment as a form of built-in governance, in which properties embodied in modified microorganisms may replace discussions and mechanisms about values and purposes of innovation. I argue that biocontainment in xenobiology can be understood as the result of a sociotechnical imaginary of *controllable emergence*, according to which controlling biological systems can ensure control over public acceptance, and governance can be enacted at the level of the organism following design principles. In the previous chapter I argued that xenobiology can be understood as a way of thinking about life as what is biologically possible. Such an imaginary of life unbound is connected to the idea that the unnatural is the safer option, as a rhetorical device to claim the legitimacy of xenobiology.

Synthetic biology has been characterized as following engineering design principles.<sup>102</sup> Scholars have debated whether engineering can be applied to biology and the kind of social practices and modes of organization this constitutes, including regimes of intellectual protection (Calvert, 2008) (cf. **Chapter two**). Just as artefacts have politics (Winner, 1986), design principles that determine what properties should be programmed in an organism are value-laden. According to Adrian Mackenzie (2010: 182), “Design principles cover over a multitude of heterogeneous dynamics and connections, and above all, conceal the strong connections between conceptions of design and ethical framings of action.” Constructing novel forms of life incorporates normative questions about what type of society new organisms would enable and whether it would be desirable, but as I argue in this chapter, design principles oriented toward achieving ‘full safety’ can restrict the scope of deliberation on ethical issues.

Even though Ben Hurlbut (2017) does not consider the feasibility of biocontainment crucial in analysing the politics of emerging biotechnologies (like gene editing), the question itself is relevant because among the visions of xenobiology is developing biocontained organisms. Understanding the materiality of biocontainment is useful for understanding its rhetoric. Scientists agree that xenobiology would provide the best containment possible. For synthetic biologists Wright and colleagues (2013: 1230), “The use of XNA *in vivo* is, however, many years away.” Or decades, as they later clarify. They refer to technical details, such as

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<sup>102</sup> For a discussion of design as an essential feature of engineering training and thinking, see Mitcham, 1994: 20.

the need to develop XNA to XNA replication and compatible XNA-compatible replication and transcription, to account for their scepticism. Despite predicting slow and unlikely progress they maintain the following:

Although only theoretical at this stage, such a system should represent the *safest biocontainment mechanism possible* through the incorporation of both trophic and semantic containment (Marlière, 2009) (ibid, p. 1230) (emphasis added).

The principal investigator at the laboratory I studied explained to me that it would take many years before xenobiology approaches could be implemented, perhaps even a decade. It is possible that what xenobiologists seek to accomplish in the laboratory works on paper but not in practice. Establishing the safest biocontainment mechanism rests on negotiating competing visions of what safety means for genetically modified organisms, as well as what forms of authority can assess and define safety. Biocontainment also begs the questions, what level of safety is enough? And what is the meaning of safety? If absolute containment can be achieved, what would it mean for questions of governance and participation?

In this chapter I examine the role that imagination plays in the framing of containment and risk. As discussed in **Chapter four**, xenobiologists advance a sociotechnical imaginary of *life unbound* that guides the agenda of xenobiology. In what follows, I address the imagination of scientists about the consequences of rethinking life. As xenobiologists work hard reimagining life, they tend to display a narrow disposition to imagining risks and undesired effects of ‘other forms of life’ (Hurlbut, 2015c). Scientists are confident that ‘certainty of containment’ could be achieved, xenobiology would serve as the *ultimate safety tool* (paraphrasing Markus Schmidt’s paper of 2010). Sheila Jasanoff has warned against the failure of imagination of risk. In the context of the 9/11 terrorist attack, she wonders how was it possible that security agents did not conceive that an airplane could be used as a weapon for massive destruction?<sup>103</sup> The imagination behind biocontainment implies ignoring alternatives to framing biosafety as the predominant imagination of governance follows an asymmetry of risks and benefits (Hurlbut, 2015c). In particular, pioneers of xenobiology follow the assumption that genetically modified organisms can be deployed out of the laboratory in a controlled manner by virtue of reimagining the relation between the natural and the unnatural, defining the latter as safe (**Chapter four**), while at the same time providing little room for imagining what can go wrong, or what needs to be foreseen. The certainty of containment and the confidence (or illusion of safety) this brings to release organisms is associated with the emergence of technology in an acceptable manner by society.

I first provide in **section 5.2** an overview of the early history of genetic engineering, focusing on the developments that led to the Asilomar Conference of 1975 in which

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<sup>103</sup> Personal communication in 2017.



molecular biologists gathered to discuss appropriate measures to handle recombinant DNA. I suggest that the vision of governance that originated in Asilomar, materialized into a vision of design: solving governance problems with technical solutions. Subsequently, I claim that such a vision (and sociotechnical imaginary) has permeated xenobiology because the design principles that lead to safety have been laid out as a scientific challenge, appealing to scientists working in the field.

Afterwards, in **section 5.3**, I argue that designing for safety conveys a particular imagination of what counts as risk and how risks can be managed, and how one effect of this type of design thinking excludes discussions around values and political aspects. Biocontainment involves a way of thinking and imagining risk, that constrains behaviour and predisposes certain actions and practices. In **section 5.3.1** I highlight the rhetorical power of the vocabulary used in xenobiology, addressing terms that express safety associated with biotechnology, like orthogonality, genetic firewall, and escape. As a whole, the use of these terms construct a discourse that helps reify xenobiology as a discipline of safety. I take a step further in **section 5.3.2** to note that in the laboratory, the imagination of risk I propose is ancillary to the work of the laboratory. Inside the laboratory, researchers emphasize how to make things work rather than deliberating about the relationship between design, responsibility, and governance. Lastly, in **section 5.4**, I discuss that the properties of safety that scientists embed in microorganisms do not only serve to provide safety (in a narrow sense) but restrict the use of microorganisms in ways that are relevant for other dimensions of governance, such as intellectual property. In what follows I argue that the recommendations of the 1975 Asilomar conference turned into a scientific agenda that has shaped efforts in xenobiology, which requires me to provide a brief historical context on the early history of molecular biology that crystallized imaginaries and ambitions that remain current to this day.

## 5.2 The legacy of Asilomar

Xenobiologists draw on debates that have remained unsettled since the beginning of genetic engineering to position safety as a desirable goal. Ever since, scientists aim to realize the vision of biocontainment established in the 1975 Asilomar conference (Hurlbut, 2015c), managing with technical means a problem that is inherently a question of governance. In what follows, I expand at length on the history of genetic engineering and its milestone of the Asilomar conference, drawing on various authors that have addressed the subject in depth. Such discussion is important because the questions that were asked at the time remain current for xenobiology, and as I argue, xenobiologists today draw on the legacy of

governance of Asilomar and aim to provide a technical solution for such vision. Since the dawn of molecular biology, it has been a priority to develop biocontained organisms, including the *E. coli* strain *Chi 1776*.<sup>104</sup> Xenobiology is advantageous because in principle, it would not be possible for an organism to mutate and return to a previous (non-contained) state, a common critique of containment mechanisms based on DNA, like ‘kill switches’ (cf. Torres et al., 2016; Wright et al., 2013). How the debate over the emergence of genetic engineering was framed is essential to understand synthetic biology and xenobiology. The 1975 Asilomar conference marked a historic milestone; its outcome influenced the subsequent development of genetic engineering and the thriving biotechnology industry. Susan Wright (1994) explains in her seminal work on the social history of genetic engineering how the formation of genetic engineering policy was a political process shaped by complex motives and cultural conditions. Her research questions include how ethical or political issues were excluded from the discourses that emerged. Wright explains that for scientists who were leading both the research frontier and its regulation, moral debates would restrict or slow down research. Scientists feared the loss of freedom to determine their research agendas as well as the slower pace of research.

### 5.2.1 The road to Asilomar Genetic engineering in the 1960s and 1970s

Understanding the historical context in which genetic engineering was embedded, particularly through the lens of the 1975 Asilomar conference, is important for the analysis that follows. The imaginary of governance I expand in this chapter has roots in the events of the 1960s and 1970s, in which dominant discussions about genetic engineering were restricted to risk, manageable in the laboratory. Safety in genetic engineering became a hot topic of dispute and policy making in the 1970s, even more than ethics (Krimsky, 1984). The decade of 1960s transitioned to the 1970s with a plethora of conflicting issues, such as nuclear proliferation, political instability brought by the Vietnam war, and environmental issues associated with the use of pesticides. Discourses about genetic engineering captured public attention. For instance, after isolating a gene from the chromosome of a living organism in 1969, molecular biologist Jonathan Beckwith (member of the organization *Science for the People*) took advantage of a press conference to warn about the dangers of genetic engineering (cf. Beckwith, 2002).

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<sup>104</sup> See Curtiss (1976). The *E. coli* strain *Chi 1776* is not viable outside the laboratory because it is not able to synthesize D-amino pimelic acid, an essential constituent of the bacterial cell wall that is not found in the environment.

Scientists such as Peter Lobban, Janet Mertz and Paul Berg of Stanford University<sup>105</sup> started to unlock the secrets that would give rise to molecular biology in the turn of the 1960s. In the early 1970s molecular biologists were pressed to show the utility of genetic engineering to politicians, so that financial support for the field would continue. At the time, there were reasons to be genuinely cautious about the risks that genetic engineering could bring for health and safety. Besides the expansion of the use of microorganisms in the 1950s and 1960s, research involved the use of highly dangerous biological agents, such as cancer-causing viruses (i.e., simian virus 40), a consequence of expansion in cancer research efforts; there were concerns about unsafe practices for handling pathogens. A case in point was James Rose, head of the molecular-structure section of the Laboratory of Molecular Biology of Viruses at the National Institute of Allergy and Infectious Diseases, whom in 1972 expressed concern about a potential cancer epidemic caused by SV40-adenoviral hybrids; furthermore, in March 1973 in the UK a technician in the London School of Hygiene and Tropical Medicine contracted smallpox from an experiment (Wright, 1994). In January 1973 the first Asilomar conference took place in Asilomar, a state campground in Pacific Grove, near Monterey, on the California coast, with a small group of scientists gathered to discuss biohazards of tumour–viruses and recombinant DNA, concerned about an epidemic of cancer (McElheny, 2003).

Wright's account places particular emphasis on the agency of the scientists who were in charge of establishing regulations for the field, and ultimately the terms of the discussion. The central theme of discussion in the Gordon Conference of June 1973 was concerns over hazards of recombinant DNA for laboratory workers and the public –although without strong evidence to support or deny the claims– led to a letter written by Maxine Singer of the NIH and Dieter Soll of Yale University addressed to the U.S. National Academy of Sciences. The letter (later published in *Science*) framed such hazards in technical terms and proposed that the Academy establish a committee to examine the problem and recommend actions and guidelines. This prompted the NAS to establish the *Berg committee*, chaired by Paul Berg. The Berg Committee then published a letter in 1974 in three major scientific journals, *PNAS*, *Nature* and *Science*; this letter called for three important aspects: first, a pause for some experiments. Second, an international conference to discuss lifting the pause (which would later be held at Asilomar II); and finally, a proposal to the director of the National Institutes of Health to establish an advisory committee to explore the hazards of the new field: the Recombinant DNA Molecule Program Advisory Committee (later called the Recombinant DNA Advisory Committee, or the RAC) appointed by Donald Frederickson, to develop

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<sup>105</sup> Other notable pioneers in genetic engineering at the time include David Jackson, Janet Mertz, Ronald Davis and Stanley Cohen.

procedures for minimizing hazards, and to draft guidelines for research. This move would keep the discussion on genetic engineering within scientific circles. For Wright, this was a “crucial move in reducing and restricting discourse concerning the issues surrounding genetic engineering as well as defining mechanisms for its resolution” (ibid, p. 138). Although thought to have promoted a moratorium, the letter actually proposed a ‘partial postponement’ of some experiments (ibid, p. 138) and emphasized the benefits of genetic engineering. The media coverage that ensued lauded scientists for being responsible because it would be on their own detriment to establish restrictions of their activities.

In the UK, the Ashby Committee established in 1974 was also constituted (like the Berg committee) of leading scientists and research directors. The committee finished the first British report on genetic engineering in January 1975, just in time for the conference in Asilomar. The report claimed that the benefits of genetic engineering outweighed the risks. Of importance, the *biocontainment* concept appeared for the first time in the Ashby report, after Sydney Brenner suggested to ‘disarm the bug,’ rendering bacteria incapable of surviving outside the laboratory (Wright, 1994: 143-144).

The National Institutes of Health (NIH) funded the second Asilomar conference, held in February 1975 at the Asilomar Conference Grounds, convened by the National Academy of Sciences<sup>106</sup>. The conference is remembered as having marked the beginning of an exceptional era for both genetic engineering and science policy (Berg & Singer, 1995). The roughly 140 professionals (primarily biologists, including lawyers and a handful of journalists) who attended the conference, wanted to achieve a consensus for voluntary guidelines to ensure the safety of recombinant DNA technology. Susan Wright (2001) refers to two moves made by the organizers of the conference who sought to maintain a technical discussion. First, the audience of the conference was tailored to attract mostly American scientists: only one member of a public interest organization was invited but could not attend. Additionally, there were no representatives of fields like ecology or evolutionary genetics, neither social science, or ethics. Second, the agenda was restricted “to exclude the awkward questions of biological warfare and human genetic engineering” (ibid, p. 240). In fact, David Baltimore opened the meeting by declaring two topics out of bounds: the biosecurity implications of recombinant DNA and the social and ethical ramifications of the technology, arguing that it was neither the time nor place to sustain such discussions (Wright, 1994: 153). This reflects a disposition to not ask *whether* the research should continue, but *how* it could continue.

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<sup>106</sup> For detailed accounts of the unfolding of the conference by a journalist who participated, see Rogers, 1975, 1977.

### 5.2.2 The legacy of governance of Asilomar

Some scientists see the legacy of the 1975 Asilomar conference as successful: a display of responsibility from scientists who stood up to the ethical and regulatory challenges of their time. Its legacy is important for understanding the research agenda of xenobiology. Commentators on the governance of genetic engineering approach the legacy of the Asilomar conference from two angles: one looking at the past, and a second looking at the present. It is a historical reference of how questions of power and authority converge with questions about science and risk, raising the question of what mechanisms should be put in place to decide the technological paths to follow. For Ben Hurlbut (2015a: 12), “The legacy of Asilomar lies less in its scientific achievements than in its implications for democratic governance of science and technology.” According to Susan Wright (2001), Asilomar was important because it allowed the scientific community to achieve consensus on an initially fragmented position that initially had been fragmented. Such unity was important to preserve their scientific autonomy. A coherent and transparent agenda would persuade the public that scientists were acting responsibly and in the public’s best interest. Had events turned out differently, the congress of the United States might have had to intervene in regulating genetic engineering, possibly withdrawing financial support (Fredrickson, 2001).

Shobita Parthasarathy (2016) remarks that the unfolding of the Asilomar conference, with its restricted participation and scope, represented a “missed opportunity” for addressing ethical and social concerns of biotechnology, as well as for developing governance frameworks that involve the public in decision making processes. Highlighting the importance of imagination as a collective source of agency, Ben Hurlbut (2015c) argues that the conference imposed limits on the imagination of risks by restricting debate to realistic scenarios, which effectively served to isolate other pressing issues, like military applications or ethical aspects. Imagination and our perception of what counts as a risk or an undesirable consequence precede discourses over risk and the type of actions that can be taken to manage them.

I argue that the legacy of the Asilomar Conferences has influenced the governance of the xenobiology’s scientific agenda, shaping thought about how to best govern contemporary technologies, based on the lessons of history that apply to technologies developed afterwards, like the genetic engineering of crops (Capron & Schapiro, 2001). Ben Hurlbut (2015c) analyses the conference as a manifestation, a ‘site of memory’ that is the product of a sociotechnical imaginary of ‘governable emergence’ of technology. Asilomar has played a role in the imagination of governance and science and the practices that sustain such an imaginary, with repercussions that extend to contemporary technologies like synthetic biology or animal cloning. For Hurlbut,

Asilomar is invoked because it crystallizes a widely shared imaginary of science and law—an imaginary of “governable emergence”—wherein not only is science imagined as an engine of change, but law is cast as always trailing behind and thus reactive to and potentially inhibitory of scientific progress (ibid, p. 127).

He further argues that imagination over possible risks, rewards and courses of action is prioritized to the scientific community, yielding law and public opinion subsidiary, both of which react, or lag behind, advances in new technology. Asilomar-in-memory persists in time because it favours science as a force of sociotechnical change and obeys a form of public reasoning that locates questions of new technologies in terms of their novelty and the risks they may present, questions that can only be addressed by experts (because only experts can foresee future benefits). Further, he claims that giving priority to scientists to imagine possible futures shaped by technology is a form of earning power; imagination not only conveys possible futures, but also what questions and what participants are legitimate to intervene in the process of social shaping of technology. Corollary to this imaginary is a restricted role for the public in the shaping of technology, which are seen as a constraint for innovation and progress (Jasanoff & Kim, 2009).

In addition to becoming a site for memory, Asilomar has been a geographical and symbolic place for meetings about responsibility in science in recent years. It has been the gathering place for meetings about geoengineering (in which Paul Berg participated) that led to light rules on responsible research (Asilomar Scientific Organizing Committee, 2010; cf. Stilgoe, 2015), beneficial principles of artificial intelligence,<sup>107</sup> and has been suggested for synthetic biology (Ferber, 2004). For geoengineering, Schäfer & Low (2014) note that although inspired by the forms of governance established for genetic engineering in 1975, geoengineering has assumed a more inclusive narrative of governance mechanisms and issues at stake, since it has benefited from wider opportunities for deliberation and framings based on multiple reports, meetings and workshops.

Asilomar has come to represent a mode of organizing discussions about ethics and futures brought by new technology, by determining in advance what groups of experts have the capacity and authority to determine which issues deserve discussion. This raises questions of self-interest of participants, and representation, in terms of those who are not invited to participate and are excluded from the ensuing discussions. These questions highlight the separation of experts and lay people, and the inequality in who gets to frame issues and matters of concern.

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<sup>107</sup> See <https://futureoflife.org/bai-2017/> [last visited July 29, 2018].

### 5.2.3 Legacy of Asilomar as design principles

The legacy of Asilomar has influenced the goals of xenobiologists with the of incorporation of governance mechanisms in synthetic organisms as built-in-safety features. Paul Berg looking back in 2004 on the thirtieth anniversary of the Asilomar conference<sup>108</sup> addressed known criticisms of the conference such as restricting the debate to biological hazards and health, excluding ethical considerations and biological warfare. He justified these choices as a need to establish priorities, claiming the possibilities of ethical dilemmas ‘were still far in the future,’ and hazards were a more imminent issue. Relevant for our purposes, Berg claimed that the risks that concerned many in the early 1970s, are no longer valid. For him,<sup>109</sup>

Literally hundreds of millions of experiments, many inconceivable in 1975, have been carried out in the last 30 years without incident. No documented hazard to public health has been attributable to the applications of recombinant DNA technology. Moreover, the concern of some that moving DNA among species would breach customary breeding barriers and have profound effects on natural evolutionary processes has substantially disappeared as the science revealed that such exchanges occur in nature.

For Berg the discussion over the safety of genetic engineering was valid at the time but at the turn of the twentieth century the issue was already settled. The Asilomar conference, for Berg, “marked the beginning of an exceptional era for science and for the public discussion of science policy. Its success permitted the then contentious technology of recombinant DNA to emerge and flourish.”<sup>110</sup>

I argue that proponents of xenobiology have capitalized on existing debates and discourses of hazards of genetic engineering to justify their research agendas, legitimizing the development of ‘contained’ microorganisms. For instance, Schmidt & de Lorenzo (2012: 2199) write: “Asilomar laid the foundation for most of the biosafety measures in place today for both biological and physical containment. Inter alia, the conference expressed that containment should be made an essential consideration in any experimental design.” Nevertheless, this process seems to pass unacknowledged in some cases, hence the power of narratives and discourses that persist over time. Some of the scientists I interviewed were not aware of the Asilomar conference and related historical episodes (cf. Capron & Schapiro, 2001); for others, the legacy of the conference was the establishment of useful guidelines which have become common practice in molecular biology. This includes the types of strains to use in the laboratory (which are attenuated), or the establishment of Biological Safety Levels (BSL) 1–4 (see Acevedo-Rocha (2016) for the perspective of a synthetic biologist). The conference has also left a positive legacy in the collective imagination of scientists, as a

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<sup>108</sup> Berg, P. 26 August 2004. Asilomar and Recombinant DNA. From [https://www.nobelprize.org/nobel\\_prizes/chemistry/laureates/1980/berg-article.html](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1980/berg-article.html) [last visited January 23, 2018].

<sup>109</sup> Ibid.

<sup>110</sup> Ibid.

successful initiative that dealt properly with the challenges of the time. For example, 5B remarks that “it was a conversation that needed to be had.” After mentioning the recommendations for laboratory practice, he notes that “The fact that we haven’t really seen any problems is testament to the approach that was taken.” It may not be surprising that scientists think of Asilomar as a site of regulation and guidelines. It established a trajectory that has ensured the success of genetic engineering without negative consequences and preserving scientific autonomy. Some see it as a triumph of the scientific community, like interviewee 19B, whom after referring to the moratorium that gave rise to the conference explained,

So they had a conference where there was a set of rules and guidelines, and a sort of moratorium on doing things for a while, until certain things could be seen. So that in a way was a very good way of showing that scientists can, are clever enough to police themselves, and to actually all agree on something, and that’s what happened there.

This recognizes the sentiment of self-governance or scientific autonomy that permeated the conference. Interviewee 19B also added, referring to the democratic structure of the conference, “Everyone agreed on certain ways of doing things, or rules, and out of that, in most of the countries that then developed legislation around GM [genetic modification], was built quite a sensible legislation frame.” In this regard, David Guston (2005) argues that the procedures to reach consensus in the Asilomar conference delineated the outcome that was decided. Nevertheless, not all the researchers I interviewed viewed the conference as necessary. For example, interviewee 29A was critical of the need to have had a conference in the first place, explaining that it was not necessary given the lack of problems with genetically modified organisms, but remarked that it “was an act of responsibility of the scientific community.”

In the case of xenobiology, I suggest that the vision of governance originated in Asilomar transferred to a vision of solving governance problems with technical solutions and design principles. Managing risk was transformed into questions of how to design safer, controllable organisms. This stretch of the imagination, of both limiting what counted as legitimate concerns —excluding social and ethical issues— and devising what properties ‘safe’ genetically modified organisms should bear is remarkable, and its legacy still shapes discussions of science policy and emerging technologies. According to the summary statement of the 1975 Asilomar conference (Berg et al., 1975), the purpose of the conference was the lift of the voluntary moratorium and determining how to enable research to continue with minimal risks (in terms of biological hazards and government intervention). Implicit in the statement is the conceptualization of risk as quantifiable, manageable, and unavoidable.<sup>111</sup> For the authors this is mainly a technical problem, besides narrowing the

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<sup>111</sup> For conceptualizations of risk, see Winner (1986). Chapter ‘On not hitting the tar-baby’, p. 138-154.



scope of the discussion to risk. They state that ‘reasonable principles’ to deal with potential risks include the following: “(i) Containment be made an essential consideration for the experimental design” (ibid, p. 1981), and that the level of containment should match the estimated risk. Among the highlights of the statement is the distinction between biological and physical barriers for containment, and the suggestion of biological risk levels (from 1 to 4) with their corresponding physical containment levels (i.e., facilities with certain capabilities of isolation of microorganisms, like air locks of negative pressure environments). Notably, the statement also suggests design principles that are proposed for xenobiology. The authors note,

The most significant contribution to limiting the spread of the recombinant DNAs is the use of biological barriers. These barriers are of two types: (1) fastidious bacterial hosts unable to survive in natural environments, and (ii) nontransmissible and equally fastidious vectors (plasmids, bacteriophages, or other viruses) able to grow only in specified hosts (ibid, p. 1982).

These two principles are followed by proponents of xenobiology (i.e., Herdewijn & Marlière, 2009; Schmidt, 2010) for whom risk and biosafety are framed as a problem of proliferation and horizontal gene transfer. These cultural and epistemological commitments rely on an imagination of risk (in the scientific community) and a consequent solution to the problem of biosafety. Such norms of what counts as safety have remained virtually unchanged in the decades following the Asilomar conference (cf. Hurlbut, 2015c), partly because they are a challenge that can be solved in the laboratory with an epistemic culture of molecular biology that favours reductionism (see **Chapter seven**). Further, the summary statement (Berg et al., 1975) included a section on implementation which suggests a technical vision of safe engineering. One recommendation is the development of ‘safer vectors and hosts’, after the conference helped to realize,

Special bacteria and vectors which have a *restricted capacity to multiply outside the laboratory* can be constructed genetically, and that the use of these organisms could enhance the safety of recombinant DNA experiments by many orders of magnitude.” (Berg et al., 1975: 1983). ... further adding that “[h]igh priority should also be given to research that could improve and evaluate the containment effectiveness of new and existing vector-host systems (ibid, p. 1984) (Emphasis added).

The legacy of Asilomar as the determination of design principles extends to other concerns for safety in molecular biology, such as measuring the ‘escape’ of genetically modified organisms. In the summary statement of the conference, the authors note that “[w]ork should also be undertaken which would enable us to monitor the escape or dissemination of cloning vehicles and their hosts” (Berg et al., 1975: 1984). Moe-Behrens and colleagues (2013) note that regarding the possibility of environmental incidents caused by synthetic organisms, “effective forensic tools would be critical for distinguishing synthetic from natural organisms and determining what role, if any, the synthetic organism played in

the incident.” They refer to ‘tracking techniques’ like ELISA<sup>112</sup> or PCR<sup>113</sup> and other approaches to track synthetic organisms. Amy Gutmann, former chair of the U.S. Presidential Commission for the Study of Bioethical Issues, displayed concern over tracking (or monitoring) escape in an interview with science journalist Jef Akst<sup>114</sup> (for *The Scientist* magazine) about the recommendations of the report of the 2010 Presidential Commission for the Study of Bioethical Issues on synthetic biology:<sup>115</sup> “We’re likely to recommend that new organisms when they’re created should be marked or branded in some manner to be able to monitor development in synthetic biology.” This follows a prevalent rationale in the field of risk assessment that risks are knowable, quantifiable, and traceable.

The Asilomar conference left a vision that incorporates a form of handling sensitive issues surrounding genetic engineering which explains why the vision has proven so stable. Biocontainment as a solution for safety turned into a challenge to be addressed in the laboratory, and proponents of xenobiology mobilize this conception to draw attention to their field. Researchers who work in xenobiology feel motivated by the challenge of doing what seems impossible, the possibility of solving a very difficult scientific problem. The combination of a scientific problem with a problem of safety leads scientists to ask —can we do it?<sup>116</sup> can we provide the ultimate solution to a fundamental problem in genetic engineering?— as an interviewee expressed. Herdewijn & Marlière (2009: 793) have invited others to join the challenge, the thrill. They conclude that “this postulate [of the impossibility of XNA-based organisms to ‘escape’] should *incite synthetic chemists and geneticists to take up the challenge*, diversify nucleic acid scaffolds *in vivo*, and hence access a safer level of informational transactions in engineered life forms” (emphasis added); noting that this means the development of XNA nucleic acids and an ‘orthogonal episome.’ This is a challenge that xenobiology is in an excellent position to address, as Schmidt & de Lorenzo (2012: 2204) write: “Although it is early days, xenobiology might solve the ultimate challenge of providing reliable *Certainty of Containment* via a genetic firewall” (Emphasis added). Pioneers, or vanguards of xenobiology like the authors above, make the invitation to addressing an ‘ultimate challenge’ appealing, because as a challenge it has matured over decades in the community of molecular biologists; it serves as an *origin story*, which turns

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<sup>112</sup> ELISA stands for enzyme-linked immunosorbent assay. It is a test that uses antibodies and color change to identify a substance.

<sup>113</sup> See footnote 85.

<sup>114</sup> See Akst, J. 2010. Q&A: Ethics chair on synthetic biology. Retrieved from <http://www.the-scientist.com/?articles.view/articleNo/29368/title/Q-A--Ethics-chair-on-synthetic-biology/> [last visited 24 October 2017].

<sup>115</sup> Presidential Commission on Bioethical Issues in Biomedical Research. 2010. “New Directions: The Ethics of Synthetic Biology and Emerging Technologies.” Washington, D.C.

<sup>116</sup> As Ian Malcolm said it in the film *Jurassic Park* (1993), “your scientists were so preoccupied with whether or not they could, they *didn’t stop to think if they should*” (emphasis added).

biocontainment into a legitimate challenge. In a similar way as expectations and promises operate, establishing a challenge can attract resources to what could become a burgeoning field. As a challenge, it may resonate with the scientific identity of potential researchers as part of a moral economy of xenobiology.

Other researchers have followed the legacy of Asilomar as a challenge of achieving containment, although not necessarily moved by pioneers of xenobiology. For example, researchers from the laboratory of Farren Isaacs in Yale<sup>117</sup> write in their article on genetic recoding of bacteria (Rovner et al., 2015: 89),

Over the past decade, synthetic biology has fuelled the emergence of GMOs with increased sophistication as common and valued solutions in clinical, industrial and environmental settings, necessitating the development of safety and security measures *first outlined in the 1975 Asilomar conference on recombinant DNA* (emphasis added).

Then they frame safety as a challenge of design: “biological barriers limiting the spread and survival of microorganisms in natural environments—*remains a defining challenge*” (emphasis added).

The question of why a set of visions established over forty years ago is still relevant for new biotechnology is intriguing. Until recently there were no technologies that fulfilled the vision of Asilomar of biological containment, although efforts have been made since the 1970s: a plethora of approaches have been developed, like kill switches, or ‘modular plasmids’ (Wright et al., 2013), but these are all subject to the criticism that organisms can mutate and hence ‘escape’ their containment. If the vision is not accomplished technically and its goals, or framing, remain the same, then it is possible that the vision persist over time, as an ideal to attain. Second, bringing attention to Asilomar helps us realize that xenobiology and its relative, synthetic biology, are caught in debates that have not changed much over time. Since the dawn of genetic engineering scientists have been manipulating life to various degrees and categories, but the practice has remained the same, altering the existing natural order. Benner & Sismour (2005: 541) comment that “[m]uch of what is currently called synthetic biology is congruent with the recombinant DNA technology discussed in Asilomar 30 years ago.” They add that “[p]lacing a new name on an old technology does not create a new hazard.” The unifying theme that connects the recommendations of the Asilomar conference with current efforts in xenobiology is the ideal, or the imaginary, that living organisms can be controlled (or kept separate, purified) and the more restricted the safer—and their actions programmed by their designers.

While pioneers of xenobiology aim to materialize a vision of safety-by-design, they co-produce a vision of governance, according to which the locus of contestation and action is

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<sup>117</sup> Note that these researchers may not identify themselves as xenobiologists, but their research goals fall into the agenda of xenobiology as an emerging field.

the genetically engineered microorganism, because all possibilities for manoeuvre can be embodied unidirectionally in the microorganism, obviating the need for further institutional apparatuses. Biocontainment also does work as a *symbol* of control over life, which preserves an allocation of responsibility and authority over scientists to maintain their determination of what counts as risk, as safe, and as important matters to discuss in the emergence of the life sciences. That xenobiologists have appropriated the vision of governance-design established in Asilomar attests to the efficiency of the conference in sealing controversial issues over molecular biology, to be managed with design principles.

### 5.3 Imagination of risk

How scientists think and imagine risk determines how they manage it. In what follows I argue that confidence of xenobiologists in embedding safety features in genetically modified organisms may lead to ignoring wider questions about what safety means in genetic engineering. The discourse of safety of xenobiology is self-fulfilling because if safety-by-design is sought and achieved, the task of governing its risks gets accomplished. Achieving full safety, however, is an illusion that needs to be maintained. An example from discussions on gun control in the U.S. is pertinent: “owning a gun certainly gives you the feeling that you are doing something –taking control– to protect yourself, and any risk is less frightening if you think you have some control over it.”<sup>118</sup> Hence, embedding biosafety features may provide scientists and potential users of biotechnology with a feeling of controlling organisms and engaging in experiments and activities that otherwise would not be conducted. Imagining risks has two consequences: first, to ignore potential sources of risks, often external. And second, altering patterns of behaviour and practices that may lead to increased risk or the neglect of fundamental issues about values and the public good.

Biocontainment is a ‘nail’ that the ‘hammer’ of xenobiology can hit, because imaginaries behind xenobiology are about isolation or extending bridges between different biological worlds. Similar to other applications of synthetic biology and biotechnology, transformations are enacted at the level of the organism, instead of a network or a system. A member of the laboratory explained to me that the incorporation of successive genetic mutations would ‘lock’ a synthetic microorganism into depending on XNA nutrients for survival (referred to as *auxotrophy*) (see **Chapter one**), which would work because this involves many layers of mutation that are highly improbable to overcome by random mutation. Confidence in the inevitability of escape is theoretically sound, but it can risk paying attention to unknowable

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<sup>118</sup> Ropeik, D. 2012. Gun Control: It's Really About Guns as Symbols, Not Weapons. *Psychology Today*. Dec 18, 2012. Retrieved from: <https://www.psychologytoday.com/blog/how-risky-is-it-really/201212/gun-control-its-really-about-guns-symbols-not-weapons> [last visited July 31, 2018].

events. However, scientists are confident in that exceptional events are not likely to be observed. Again, the film *Jurassic Park* provides a good setting for thinking about scenarios outside planned risks (cf. **Chapter one**). For instance, Benner & Sismour, (2005: 541) write,

By contrast with the power of Darwinian processes implied by the *Jurassic Park* principle ('life finds a way'), Darwinian processes are highly conservative when it comes to creating new functions. When tackling new problems, Darwinian systems take small steps from what they already have; they are not innovators on a large scale.

I raised this possibility of 'life finding a way' in the first discussion I held with the laboratory group, in one of its weekly meetings<sup>119</sup> (see **Chapter three** for details). I presented to the group an interview between science journalist Ira Flatow and Dan Mandell about their recent work in developing semi-synthetic organisms (Mandell et al., 2015) to the group. During the interview Ira Flatow played a segment of the film *Jurassic Park*<sup>120</sup> (released in 1993), which I showed the group.<sup>121</sup> In the video, Dr. Henry Wu, the geneticist that brought the dinosaurs back to life, explains to the visitors of the park that all the dinosaurs in the park are female, unless scientists supply them with a hormone at the right developmental stage. Then the mathematician Dr. Ian Malcolm responds by saying,

If there is one thing that the history of evolution has taught us is that *life will not be contained, life breaks free*, expands to new territories and crashes through barriers painfully, maybe even dangerously, but... (Emphasis added).

Dr. Wu then insists of the impossibility of the females turning into male, to which Dr. Malcolm further adds the now famous phrase: "I'm simply saying that *life finds a way*" (Emphasis added).

In the laboratory discussion researchers were pleased to see an example of biocontainment in popular culture, which some had not recognized previously. They found the film sequence amusing, which is understandable given the 'retro' look of the film being watched over twenty years after it was filmed. A postdoc in the laboratory commented that 'life breaking free' should not be a concern in the paper discussed during the same session (Mandell et al., 2015), since several different mutations were being incorporated in the modified organisms of this study. Another scientist commented that escaping containment is a remote possibility, and '*certainty of containment*' could be achieved (cf. Schmidt & de Lorenzo, 2012). This referred to the impossibility of organisms escaping the containment because Mandell and his colleagues in George Church's laboratory incorporated various

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<sup>119</sup> Part of the discussion involved the interview with Dan Mandell and Dave Guston by Ira Flatow, in the radio show 'Science Friday' (released January 23, 2015). See <http://www.sciencefriday.com/segment/01/23/2015/scientists-engineer-bacteria-with-genetic-kill-switch> [last visited 31 January 2018].

<sup>120</sup> Sarah Franklin (2000) argues that life itself is re-imagined in the film *Jurassic Park*, mixing science and spectacle.

<sup>121</sup> Available in YouTube, see <https://www.youtube.com/watch?v=ojjEsqT2QKQ> [last visited 31 January 2018].

mutations in the biocontained cells. A postdoctoral researcher reminded the group that in an island inhabited by female dinosaurs, there could be no way of procreating.

What I sought to accomplish with the discussion was to challenge the confidence of the researchers in managing hazards with biocontainment. The plot in the first Jurassic Park film is driven by external factors outside the agency of the dinosaurs. The park failed because an employee dismantled the park's security system, not because the containment measures failed. The park's computer programmer, Dennis Nedry is bribed by the parks' competitors to steal fertilized dinosaur embryos. In order to do so, Nedry deactivates the park's security system to gain access to the embryo storage room; as the electricity goes out, the park's electric fences are deactivated, allowing dinosaurs of the park like the *Tyrannosaurus rex* and the velociraptors to wreak havoc. This shows us that imagining risks and the ways to manage them are intrinsically limited, as risk is the interplay of multiple factors, including human agency –or what biosecurity scholars would call 'misuse.' Following the narrative of scientists, theoretically with xenobiology no mutations could allow synthetic xeno-organisms to escape their containment. In the context of Jurassic Park, this makes it difficult to address ask about measures that should have been taken if the dinosaurs escaped their containment. Building something just because it is possible can bring trouble. Jack Stilgoe also draws lessons for RRI from the film franchise, when he writes,<sup>122</sup>

It is easy to forget that the key to Jurassic Park's downfall was old-fashioned personal greed. The dreams of a philanthropreneur, imagined as naïve but pure, were undone by an employee's plan to steal genetic secrets. In Jurassic World, another billionaire with no wish other than to create joy has unwittingly employed a man who wants to weaponise velociraptors. The lesson for responsible innovation is that we should not ignore the connections between science, profit and power.

The commitment of researchers to achieving safety by incorporating safety features in engineered organisms should come as no surprise. They are led by an imaginary of 'controllable emergence,' according to which control (and by extension, domination) in biology is possible, and experimentation in biology is considered an effort of controlling variables and parameters of living organisms. The laboratory is constituted as a separate space from the real world, in which properties of living organisms can be reduced to a few parameters that the experimenter can vary. Making an experiment 'work' involves trusting that all that could go wrong, or that is unknown can be left out of the process, leaving only relevant parameters that are controllable. Concern over 'unknown unknowns' has received attention by STS analysts (cf. Stirling, 2010; Wynne, 1992). Fully controlling engineered organisms might work on paper and as a theoretical framework, but in practice it is necessary

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<sup>122</sup> Stilgoe, J. 2015. Jurassic World: Frankenstein for the 21st Century? *The Guardian Political Science*. Retrieved from: <https://www.theguardian.com/film/political-science/2015/jun/24/jurassic-world-frankenstein-for-the-21st-century> [last visited 31 July 2018].

to account for the unexpected. Confidence in achieving ‘certainty of containment’ implies that questions of governance that could be handled by other means tend to be ignored, because it provides strength to the argument that if genetically modified organisms are safe (in theory), as determined by scientists that have had the authority to set the terms of the debate, then there are no strong reasons to worry about their existence or their impact in society. This is in line with the assertion that the question around biocontainment is both ontological as well as part of the regime of governance set in motion (Hurlbut, 2017b). How researchers imagine, frame and respond to perceived risks depends much on the vocabulary available to understand the system that can lead to negative outcomes. In what follows I provide an overview of the terms and meanings that xenobiologists have used to portray their promise of creating *safe* genetically modified organisms. Creating such vocabulary helps to reify the illusion of safety that xenobiology seeks, drawing on existing imaginaries of governance.

### 5.3.1 Vocabulary of safety

The efforts of xenobiologists to position the problem of safety as a worthwhile endeavour for which they can offer the best tools available involves developing a vocabulary for this association, that reflects an ‘imaginary of controllable emergence’<sup>123</sup>. In this section I show some of the concepts that serve as rhetorical tools to portray xenobiology as safe. Some of these concepts are already found in the life sciences, whereas others are the result of xenobiologists’ efforts. Notably, the work of Steven Benner that has provided the pillars of xenobiology has focused on the development of ‘artificial genetic systems’ and new polymerases that can support them (Benner, 2004: 626),<sup>124</sup> does not associate the field of alternative genetic systems with the development of safe-by-design systems (see **Appendix one**). The association between xenobiology and safety deserves attention, since work must be conducted by scientists to establish it and maintain it. The terms detailed in the paragraphs to follow —orthogonality, genetic firewall, genetic pollution, and escape— are elements that serve to illustrate the constructed nature of biocontainment.

The concept of *orthogonality* has been used to distinguish xenobiology from other subdisciplines of synthetic biology. For example, the European ERASynBio initiative<sup>125</sup> in

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<sup>123</sup> This related to the ‘problem of choice’ (Zuckerman, 1978) that refers to how scientists select problem areas in which to work and specific problems within them. A criterion for identifying a scientific problem involves that the problem is considered amenable to investigation.

<sup>124</sup> It is recent that xenobiology, as a recent emerging field, seeks to be associated with the solution for the safety of GMEs –by means of containment–. As explained above, Steven Benner, pioneer of the field, has not made such association (i.e. Benner & Sismour, 2005).

<sup>125</sup> See footnote 54.

the report *Next steps for European synthetic biology: a strategic vision from ERASynBio* (ERASynBio, 2014), refers to genetic recoding (one of the goals of xenobiology) as ‘orthogonal biosystems’ (**Figure 8**). The term is drawn from geometry to imply a perpendicular association. By extension, orthogonality is also used to refer to the separation of specific features of a system. Moe-Behrens and colleagues (2013: 6) define the concept as “(greek: orthos–“straight,” and gonia–angle) Modification of one component of a system that does not propagate side effects to other components of the system.” The authors note that the “orthogonal life form approach uses biochemical building blocks (i.e., nucleic acids and amino acids) that are incompatible with natural cells” (ibid., p. 6), associating the concept with isolation or distance from natural systems (or unnaturalness), as addressed in **Chapter four**.<sup>126</sup> Synthetic biologist Víctor De Lorenzo (2011: 5) shares this interpretation of orthogonality as an independent genetic system:

The term orthogonal (borrowed from mathematics and computer science) is again a powerful allegory that implies a factual independence between otherwise co-existing systems. ... while the term orthogonal means independent, when used in the synthetic biology literature it largely denotes a lesser dependence of the host’s native programs.

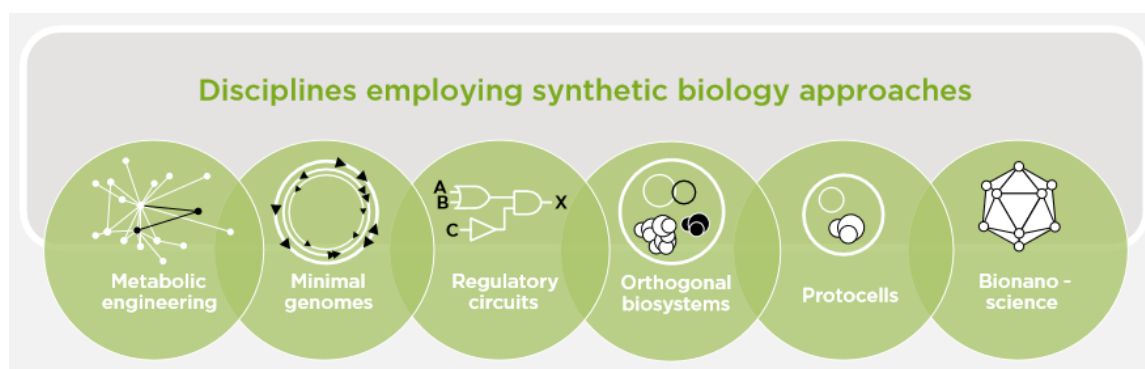


Figure 8. Disciplines employing the synthetic biology approach. Note that ‘orthogonal biology’ is among those listed, which can also be understood as xenobiology. Adapted from ERASynBio (2014: 7).

Orthogonality is the basis for claims that xenobiology–based organisms are safe for the environment, because it stands for the possibility of separating, or isolating, synthetic organisms from natural organisms. In a lecture in February 2015 at University College London for the event titled ‘I Think, I Make: A Conversation on the Origin and Future of Life’, synthetic biologist Vitor Pinheiro explained orthogonality as a:

Great way to provide biocontainment, because what you are trying to do is come up with something that can work with biology, or in biology, but cannot interact with nature, so you can sort of try and isolate it altogether.

<sup>126</sup> In **Chapter eight** I refer to a discussion about orthogonality in a panel with synthetic biologists and an STS analyst.



He further added that xenobiology is about “trying to create an alternative for biological processes. One we can maintain contained.”

Another concept related to safety is ‘*genetic firewall*,’ a barrier for the exchange of genetic information between organisms that possess different genetic systems; it would make communication or the transfer of genetic information impossible between species. Recruiting an information systems metaphor, Markus Schmidt (2010: 326) suggests that such a firewall could limit ‘genetic interaction’ with the natural world, effectively providing an ‘isolated genetic enclave within the natural world.’ This framing means that the main threat that genetically modified organisms may present exchange is the transfer of genetic information, rather than the interaction of synthetic organisms with natural ones (**Figure 9**). Addressing horizontal gene transfer has been at the heart of debates about the safety of GMOs (Gupta, 2013; National Research Council, 2004) and the target of biocontainment principles.

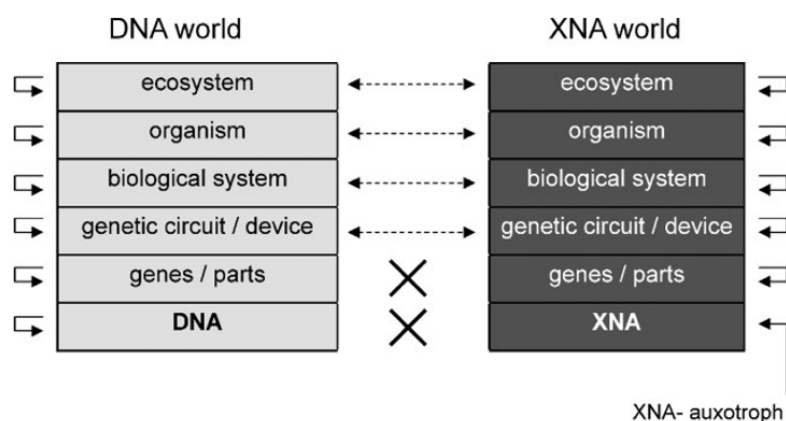


Figure 9. Scheme representing the impossibility of transmission of genetic information (a ‘genetic’ firewall’) between natural organisms and XNA-based ones (Schmidt 2010: 328). In the caption of the figure, Schmidt writes ‘A small step for a molecule, but a big step for safety.’ (ibid: 328), relating the ‘XNA world’ to a world of safety (see chapter four).

The metaphor of a firewall, also referred to as a ‘semantic firewall’ (due to the blockage of information exchange) has been adopted by researchers in xenobiology. For example, synthetic biologists Acevedo-Rocha & Budisa (2011: 6961) write that “Complete genetic isolation, which is only possible with cells containing “xeno-DNA” as genetic material or alternative/different genetic codes, should prevent horizontal gene transfer between species.” Highlighting the uniqueness of xenobiology for assuming this problem and referring to the separating properties of a firewall, they add: “In this way, a *genetic firewall against the natural DNA-based world* could be established. The biosafety and biosecurity aspects of these possibilities have been extensively elaborated just recently” (ibid., p. 6961) (emphasis added). The term genetic firewall has been used in debates over regulation in synthetic biology, a concept used in synthetic biology and policy circles. In a commentary about the draft opinion on risks of synthetic biology conducted by the European Commission Scientific

Committees, Breitling and colleagues (2015: 107) write that the European Union recommended the “development of additional approaches, including genetic firewalls based on noncanonical genetic material.” Such approaches can only be accomplished with xenobiology, a field that promises control as a form of isolation. Using the term ‘genetic firewall’ as a boundary object (Star & Griesemer, 1989) allows discussions about safety in larger spheres, such as policy circles, facilitating the diffusion of xenobiology as a solution for biosafety.

Pioneers of xenobiology recruit terms already in use, in addition to proposing novel terms for discussions about safety. The undesired or uncontrolled transfer of genes between genetically engineered organisms and other species can be understood as ‘genetic pollution,’ a term first suggested by *Greenpeace*<sup>127</sup> as propaganda (in a derogatory sense). Herdewijn & Marlière (2009) use the term in the article that establishes a vision for how xenobiology can constitute a path toward safe genetically modified organisms. They write the following,

The risks of genetic pollution cannot be overlooked, considering the uniformity of genetic alphabets, the universality of the genetic code, and the ubiquity of genetic interchanges between domesticated and wild species (Emphasis added).

However, such a risk can be addressed through technology:

Technologies for preventing or restricting genetic cross-talk between natural species and the artificial biodiversity needed for scientific and industrial progress should be designed and deployed to anticipate this challenge (ibid, p. 792).

Pioneers of xenobiology recruit a term with a negative connotation for genetic engineering for the purpose of constructing a discourse about safety that can help positioning the field. One last term that deserves mentioning is ‘escape’, or the possibility that contained organisms overcome ‘genetic safeguard’ mechanisms put in place to control their growth (Moe-Behrens et al., 2013). This has been a long-standing concern for genetic engineering, which traces back to the Asilomar conference. The U.S. National Institutes of Health has recommended that the limit of engineered microbe survival or engineered DNA transmission be less than 1 cell per  $10^8$  cells.<sup>128</sup> The term escape serves to encapsulate concerns over the release of organisms into the environment in a way that can be measured, compared, and used to show the effectiveness of containment. The metaphors and conceptual tools used to refer to biosafety determine the design principles and efforts of scientists, similar to the way

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<sup>127</sup> See Genetic Engineering Briefing Pack. February 2002. Genetic pollution – a multiplying nightmare. [http://www.greenpeace.org/sweden/PageFiles/497049/genetic\\_pollution.pdf](http://www.greenpeace.org/sweden/PageFiles/497049/genetic_pollution.pdf) [last visited October 22, 2017]. See interview with Greenpeace co-founder, Patrick Moore. <https://web.archive.org/web/20061124234512/http://www.heartland.org/PrinterFriendly.cfm?theType=artId&theID=14035> [last visited 22 October 2017].

<sup>128</sup> Cf. Wilson, 1993. See also, *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. [https://osp.od.nih.gov/wp-content/uploads/NIH\\_Guidelines.html](https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.html) [last visited October 22, 2017].

that metrics and performance indicators influence institutional practices and policy responses: metrics shape behaviour and practices.

The term *escape* evokes a conception of space. It refers to escaping the containment or the measures incorporated in the organisms themselves to achieve full control. Space in this context is also defined as genetic information. A case in point is provided by synthetic biologist Dan Mandell (a post-doctoral researcher in the laboratory of George Church). In an interview with Ira Flatow for his radio show *Science Friday*,<sup>129</sup> Mandell refers to ‘*escape*’ to ensure that the systems they have developed are safe, because they tested their *escape* frequencies.<sup>130</sup> The following extract from the interview shows how *escape* frames a concern over unknown risks in terms of the possibility of controlling organisms, and uncertainty:

Ira Flatow: So how do you know that the bacteria can't just evolve their way out of this restriction? Acquire the changes necessary to live out there in the wild?

Dan Mandell: We tested them in three critical ways. The first is to make sure that they can't escape by mutating, and to test that, we grew up about a trillion different bacteria in the presence of the synthetic amino-acid, and then we take it away. We observe that none of them could survive, meaning that they can't escape the dependency by mutating their genomes, even when they're grown into large numbers of cells.

Ira Flatow questioned how confident Mandell could be of the technology he developed in Church's laboratory. But for Mandell the question is not about what is uncertain, but rather, how to achieve control, and what type of tests may be accepted as evidence of achieving that control. Scientists seem to take for granted whether what occurs in the laboratory reflects the behaviour of microorganisms in open environments.

In summary, synthetic biologists have developed and recruited terms related to safety in order to construct a rhetoric of xenobiology as a safe emerging field. Concepts are loaded with meaning, enabling a discourse of safety that creates an epistemic reality. Such reality is located at the basis of the synthetic microorganism, as a property that scientists can manipulate. Genetic pollution, orthogonality, and genetic firewalls are qualities and symbols of control that can be altered at the level of the organism, which makes them attractive for scientists to build a discourse of safety. What is interesting about the mobilization of concepts associated with safety is that xenobiologists recruit them from a pool of cultural resources in the life sciences (i.e., orthogonality, ‘*escape*’ and ‘*genetic pollution*’), meanwhile they also

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<sup>129</sup> Interview with Dan Mandell and Dave Guston by Ira Flatow in *Science Friday*. January 2015.

‘*Scientists Engineer Bacteria With Genetic ‘Kill Switch’*. See <http://www.sciencefriday.com/segment/01/23/2015/scientists-engineer-bacteria-with-genetic-kill-switch> [last visited October 23, 2017]

<sup>130</sup> See Mandell et al., 2015. It is noteworthy that their study was not based on XNA, but on genetic code recoding. Not all the synthetic biologists working on approaches that can be categorized as ‘*xenobiology*’ use concepts like orthogonality or *escape*. But these fields serve the purpose of providing a conceptual toolkit to talk about release, uncertainty and risk, in a way that is more associated with a scientific question, than a question of governance.

create terms that apply exclusively to xenobiology, such as a semantic firewall. The confluence of concepts with different meanings for the purpose of constructing a discourse of safety is interesting, because it reflects work that scientists conduct to create narrative and discourses to position xenobiology as a biosafe enterprise.

### 5.3.2 Biocontainment in the laboratory

For the argument that biocontainment is a form of imagining risks, to be enacted and managed in the laboratory as a scientific problem, it is important to take a closer look at laboratory scientific practice. Xenobiologists make promises of biocontainment because the type of research they conduct in the laboratory—mostly based on molecular biology and organic chemistry—allows them to construct biocontained organisms, insofar safety is defined as the blockage of information transfer between organisms. Simply put, biocontainment is a goal that xenobiology is well suited to achieve (in the laboratory). Pioneers of xenobiology have conceptualized the field as being artificial, and proposed that the more artificial, the safer biological systems can be.

In the weekly meetings of the laboratory research group I attended as part of my fieldwork, researchers presented advances of their projects, or ‘work in progress’ (See **Chapter three**). In their presentations and ensuing discussions, the laboratory members did not address the meaning of biosafety or biocontainment.<sup>131</sup> They assumed and understood that containment was a desirable goal, and by extension a good justification for the research being conducted. They referred to containment in technical aspects: the work required to make biological artefacts that met the required principles for safety. Participants seemed to not examine nor view problematic the idea that biocontainment could serve as an instrument of built-in governance. It was accepted and mobilized as a property of biological organisms that required to be engineered. The question in their mind was *how to make biocontainment work*, rather than the governance implications of its articulation.

In the ‘work in progress’ presentations it was common that the presenter referred briefly to biosafety and biocontainment in the introductory slides, using, for example, phrases like ‘this work is important for the goal of biosafety.’ References to containment were not meant to convince other members of the laboratory of their importance, or to situate the importance of the work being conducted. They were presented as a form of identity of the laboratory, to flag that they were working toward a common goal. Even though not all the members of the laboratory worked in projects related to biocontainment, they were aware of the motivation

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<sup>131</sup> However, the principal investigator of the lab once explained in a presentation of his vision of the lab, that biosafety had played an important role in securing major grants for the lab.

for this end. In a ‘work in progress’ presentation, a student in the laboratory presented their work on developing a synthetic orthogonal assembly of molecular machinery,<sup>132</sup> a unit of DNA capable of replicating autonomously within a suitable host. In the introductory slides, one displayed: “orthogonality is essential for: [in bullet points] function of the synthetic [molecular machinery], biocontainment, *in vivo* directed evolution.”

In a related episode, a post-doctoral researcher of the laboratory presented work related to the engineering of an assembly of molecular machinery based on XNA. The researcher started providing an overview of the XNA assembly of molecular machinery in which two slides were devoted to explaining the justification for such a machinery. It could provide a mechanism for biocontainment by enabling (through the use of XNA), first, a *genetic firewall*; and second, auxotrophy—the inability of an organism to synthesize a compound required for its growth—through the use of XNAs. The slide showed a diagram representing two cells, one using DNA and the other using XNA, the latter needed to grow and survive. This was presented relatively quickly, because these are concepts familiar to the laboratory group. Likewise, one of the technicians in the laboratory in a presentation about the engineering of a transcriptase, associated biocontainment with the goal of evolving an XNA assembly of molecular machinery, which would require three adapted enzymes: a polymerase, a replicase, and a transcriptase. The presenter included the text “aim/purpose” as “biosafety, redundancy within the system,” in a small letter size on the bottom left corner of one of the first slides.

During my fieldwork, researchers in the laboratory wrote and published a review article about biocontainment in synthetic biology. Early in my fieldwork a postdoc in the laboratory explained to me that they were writing a review about biocontainment and had a large amount of literature to read, while also suggesting that the researcher was new to that literature. I offered articles on the subject and recommended literature, some of it related to the 1975 Asilomar conference. I thought the writing of the review could provide a space to open up conversations on containment and governance, but due to time constraints, the researchers involved did not welcome the idea of having dedicated sessions to discuss the assumptions and values of biocontainment. I did not have access to draft of the review while it was being written; however, during a weekly laboratory meeting close to the submission of the review for a journal, the principal investigator asked me if I could read the review and provide feedback. The published version of the review is similar to other reviews on biocontainment that address the topic in a scientific manner, describing the state of the art of approaches to biosafety in synthetic biology. The review did refer to risk in xenobiology,

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<sup>132</sup> Technical term omitted to preserve anonymity of the laboratory. For this project, XNA materials were not involved.

noting that we lack an appropriate understanding of risk, because risk assessment requires knowing all possible outcomes.

Scientists in the laboratory follow a design plan (and a vision of governance) established in the Asilomar conference, which the scope of xenobiology is well suited to achieve. Insofar scientists conceive of containment as a design goal it is practical for them to focus their efforts on how to get there. They focus on the ‘how’ side of things (of making things work) rather than questioning the ‘why’ (cf. Winner, 1990). Biocontainment is translated into a set of design rules or goals that scientists follow, and questions are expressed in terms of *how to get there*. Even though these rules (or principles) incorporate values and forms of action in the organisms and products of xenobiology, they pass unnoticed, as the focus of the scientists is to make their experiments ‘work.’ Making projects work involve developing new enzymes, tests and protocols that can evaluate new functions, like replicating XNA, and constructing molecular assemblies that pave the road for an organism that functions based on XNA. These little steps fit well together when biosafety is framed as a problem of information transfer between organisms, supported by an imaginary of controllable emergence. In the laboratory, biocontainment is a problem of design, of ‘how to get there,’ of how to turn it into a doable problem (Fujimura, 1987). Once research projects take place in the laboratory, over many sessions of tinkering and experimentation, questions of desirability and governance are left outside the walls of the laboratory. This is due partly to the apparent lack of utility of asking such questions and because of commitment that containment can be achieved by design, at the level of the organisms, determined by the properties that researchers manage to incorporate in future synthetic microorganisms. Placing the weight of governance of biotechnological creations on design principles of containment has persisted in xenobiology because it has been framed as a scientific challenge that can be solved in the laboratory.

The scientific practice of xenobiology laboratory is a good fit for producing ‘safe organisms’ by virtue of constructing genetically engineered microorganisms with an isolated genetic system. There is little connection between the narratives of safety in xenobiology and the practices of researchers in the laboratory, which reinforces the view that biocontainment is rhetorical. Even though there is no strong correspondence between the narratives of biosafety and the work conducted in the laboratory, both have in common a predisposition for ‘control,’ in terms of exerting governance by design, and of manipulating microorganisms to the limits of what is biologically possible. Thinking of xenobiology as led by an imaginary of ‘controllable emergence’ helps to understand the mechanisms that researchers use to legitimize the field and gain acceptance for the release of genetically modified microorganisms to the environment. In the next section I discuss that the properties of safety that scientists embed in microorganisms do not only serve to provide safety (in a narrow

sense) but to restrict the use of microorganisms in ways that are relevant for other dimensions of governance, such as intellectual property.

## 5.4 Beyond biocontainment as built-in governance

In this chapter I have argued that the products and imaginaries of xenobiology can be interpreted as a form of governance by design, embodied in genetically modified organisms. The imaginary of *controllable emergence* I have introduced in this chapter concerns not only what would happen if genetically modified organisms escape the laboratory, but rather, how to ensure that they can cross the boundary between the laboratory and society legitimately (a theme I address in the next chapter). Biocontainment serves as an enabling feature of release, not just about crossing the limits life but crossing the limits of containment (what can or cannot be released). This has been a concern since the early debates on the hazards of genetic engineering; for instance, Pamela Lippe, of Friends of the Earth, warned the U.S. congress in 1977:

DNA is probably the most unforgiving technology we have yet developed. Radiation decays. We can stop making toxic chemicals. But a novel organism has a life of its own; once it has escaped or been released, once it has established an ecological niche, it is out and replicating, perhaps beyond our ability to control or clean up (Cited in Perrow, 1984: 294).

Sydney Brenner thought of ‘disarming the bug’ so bacteria would not be capable of surviving outside the laboratory (Wright, 1994: 143-144). In xenobiology, with biocontainment, new questions arise now that the ‘bug’ can be disarmed and made ready to be used in open environments. If genetically modified organisms are deemed safe to be used in the wild, this challenges existing regulations, and the terms of the boundary between the laboratory and society, to include society in experimentation with genetic engineering. Nevertheless, developing xeno-organisms does not necessarily involve developing biocontained organisms; xeno-organisms could be developed without built-in-safety features, but this would require an extended research agenda that included creating an XNA metabolism (more in the next chapter). Containment builds upon the biological impossibility of decoding genetic information in DNA and XNA formats, what xenobiologists call a ‘genetic firewall.’ Hence, xenobiology is subsidiary to containment insofar safety is defined as an issue of information transfer, or the more unnatural, the safer (**Chapter four**). Nevertheless, containment enables, or legitimizes, field release of GEMs, applications that take place outside the laboratory or factory. The vision of containment, although supported by an imaginary of governable emergence that has taken hold since the Asilomar conference, is not stable. It depends on how researchers in xenobiology continue to articulate containment as a problem that can be solved in the laboratory.

Xenobiology stands on an imagination of risks that can be managed with technology, via properties that can be incorporated in genetically modified organisms (cf. Gottweis, 1998; Hurlbut, 2015c; Krimsky, 1984, 2005; Wright, 1994). The possibility that xenobiology brings of materializing the vision of the 1975 Asilomar conference, of constructing biocontained organisms and the materialization of self-governance, is noteworthy. Even though xeno-organisms are far from being a reality, in theory they would be *certainly contained*. This can lead the development of the field through a trajectory of closing down, in which there is no incentive or need for expanding the scope of deliberation on the ethics and politics of genetic engineering. It is unknown how the dynamics of regulation and debates on xenobiology may play out given the possibility of ruling out potential hazards; will decisionmakers and the public accept the claims of biocontainment? If narratives and imaginaries of governance by containment point to a desirable future, and the technology is attained, would that change the content of the conceptualizations between science and safety?

The bottom line of containment by governance is not whether organisms can be designed to be 'safer,' but whether control over them and the multiple ways in which they may interact with their environment, can be effectively embodied in the organisms themselves. The exertion of control by means of keeping entities separate is also reflected in the study of Richard Milne (2012) of imagined geographies in biopharming.<sup>133</sup> Although the promise of producing pharmaceuticals in plants was tempting as a low-cost alternative, the need for controlled production spaces for pharmaceuticals translated to the alternative of growing plants in greenhouses, to physically contain biopharmed crops and separating them from traditional crops. Containment in xenobiology is also about the use of genetically modified organisms outside the laboratory—in the *real world*. This is where the limits of society blend with the limits of the biological, since the context in which organisms are meant to unfold and carry out their functions results the same. Scientists uses biocontainment as a tool for governance, for negotiating the barriers between the laboratory and society, and earning a license for scientists to move their organisms manipulated in the laboratory outside of the walls of the laboratory.

Biocontainment is indicative of a regime that favours the privatization of value in biotechnology. In thinking about XNA as a 'tool for governance,' safety becomes a legitimate tool to enable further uses of biotechnology, the emergence of regimes of control based on built-in features. In this sense, organisms are restricted to perform in limited ways that correspond to specific situations of concern. In focusing on the promise of biosafety through containment that xenobiology provides, we run the risk of missing attention to other

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<sup>133</sup> Biopharming is the production and use of transgenic plants and animals genetically engineered to produce pharmaceutical substances for use in humans or animals.



important aspects for governance, including ownership, access, and distribution of risks. For instance, in a study about developing ‘safeguards’ in yeast, Cai and colleagues (2015: 1803), after remarking the potential of synthetic biology to improve our living conditions, propose that,

Biosafety mechanisms should be carefully considered to minimize or prevent dual use. Professionals have chemically synthesized infectious virus in the absence of natural templates (2) and reconstitute infectious human retroviruses (3) and the 1918 “Spanish” influenza virus (5).

Moreover, they also raise awareness about another pressing issue, DIYbio:<sup>134</sup> “At the same time, relative amateurs are trying to engineer microbes in a do-it-yourself fashion ([www.diybio.org](http://www.diybio.org)).” Returning to biosecurity, they then write that measures are required to:

Minimize both bioterror (e.g., the anthrax attack in the United States in 2001) and “bioerror” (accidental environment releases or self-infection by laboratory-adapted microbes” as in the case of a laboratory infection of an individual with hemochromatosis, where the victim scientist’s high iron levels caused by hemochromatosis complemented the natural iron requirement of attenuated *Yersinia pestis*) (17).

Furthermore, the authors also suggest a role for biocontainment as a physical form of protection of intellectual property issues:

Intrinsic biocontainment can also be used to prevent industrial espionage by protecting the intellectual property of biotechnology companies.

Authors like Chan and colleagues (2015) have shared their support for the possibility for dealing with intellectual property: “In addition to its use as a biocontainment system, the Passcode circuit may find particular utility as *a tool for intellectual property protection*, where unauthorized growth of strains without the appropriate passcode molecules would induce cell death” (ibid., p. 85) (Emphasis added). Embodying and installing in organisms a restricted range of associations and possibilities is a prime example of built-in governance. This has been observed by Ben Hurlbut (2017), who argues that containment enables a ‘travelling jurisdiction’ in synthetic organisms in which the apparatus of governance and the control of the organism travel with the organism, “thereby trumping, displacing, and obviating the need for social regimes of control” (ibid., p. 79). As such, it is an efficient way of exerting governance, doing the work of conventional law.

As biocontainment is meant to enable field release it extends the use of GEMs outside the laboratory, embedded properties are mobile. This may lead to ignoring local social and political drivers for solutions whose problems are multifactorial (i.e., bioremediation), avoiding tackling and identifying root causes. GEMs are meant to be equipped to act anywhere, everywhere, regardless of the local context (i.e., the environmental conditions) and what type of users use them. In other words, containment and field release may

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<sup>134</sup> For a discussion of do-it-yourself biology in STS, see Meyer, 2013; Seyfried, Pei, & Schmidt, 2014; Tocchetti & Aguiton, 2015; Vaage, 2016.

encapsulate an assumption that ‘plug and play’ is feasible and desirable. Relationships matter between the land, local cultures and practices, users and experts.<sup>135</sup> The traveling property of containment turns xenobiology into a ‘one size fits all’ approach, fit to produce standardized, simplified organisms that can (in principle) function anywhere, in a generic fashion. The vision of an *in vivo* xenobiology does not pay attention to the context in which xeno-organisms would play out. Standardized organisms are by definition easier to produce in large scale, desirable in a context of pressure to translate science at a fast pace.

In summary, recent studies in biocontainment reflect an underlying imaginary according to which design principles can be used to deal with pressing issues of governance in a controlled and efficient manner. Such aspirations not only invite scrutiny in terms of the likelihood of their goal (such as being effective in ensuring intellectual property protection) but deserve exploring the assumptions according to which they operate. Before assuming a position on whether it is appropriate or not to deal with intellectual property or biosecurity with the properties of organisms, what matters is the hubris shown in having modified organisms acting as tools for governance. This not only illustrates that the debates on biocontainment are not only about safety and public acceptance, but also, what means (both technical and social means) should be employed in governing synthetic biology (and xenobiology). This should spark a sensibility to think about containment not only in terms of safety, but also about the discourses and motivations mobilized behind the label of containment.

## 5.5 Summary and conclusions

The safety of genetically modified organisms has been a concern since the dawn of genetic engineering in the 1970s, leading to a moratorium in 1973 that was addressed in the 1975 Asilomar conference, in which leading scientists gathered to discuss how to advance research in molecular biology safely and responsibly, a display of self-governance. Containment is about developing technological capacities to administer death (as well as life) and managing the cycle of life. Biocontainment is a symbol of control over life which preserves an allocation of responsibility and authority over scientists to maintain their determination of what counts as risk, as safe, and as matters that deserve discussion in the emergence of the life sciences.

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<sup>135</sup> See Stirling, A., Ely, A., and Marshall, F. (2018, February 8) How Do We ‘Co-Produce’ Transformative Knowledge? [Blog post]. Retrieved from <https://steps-centre.org/blog/how-do-we-co-produce-transformative-knowledge/> [Last visited April 12, 2018].

As I show in this thesis, researchers seek to associate xenobiology with responsibility through (bio)safety.

Biosafety in synthetic biology has not received much attention in the STS literature. It was not until recently that some pioneers of xenobiology have made promises of safety, following their adoption of an imaginary of governance that has been around decades earlier. For these pioneers, xenobiology is the best solution for biocontainment, recruiting in the process the visions and discourses of governance that predecessors in molecular biology established. The materiality of xenobiology should not be treated as separate from its social developments. In the first section of this chapter I provided an overview of the early history of genetic engineering, based on previous accounts (Krimsky, 1984, 2005; Rogers, 1977; Wright, 1994). I highlight that in the early days of the nascent field, scientists narrowly framed the ethical, social and political implications of genetic engineering as a subject of risk management. The vision of Asilomar has laid an agenda of safety that could be accomplished with design principles (in the form of biological containment and the prevention of horizontal gene transfer) that not only could be worked out in the laboratory but was framed as a challenge to solve. Following Dan Sarewitz (1996), there are political problems that cannot be solved with science; if they could be solved with science, they would not be difficult political problems. Xenobiology continues a trend that has lasted for decades of framing the associated political problems of genetic engineering as a problem of safety, ignoring other considerations, such as promoting inequality, the distribution of benefits, altering the balance of nature, and other rationales. Hence it is important to note when biocontainment can substitute mechanisms of governance that rely on political modes of organization and representation, as well as enforcing governance by means that exclude political instruments, like enforcing intellectual property protection in biocontained organisms.

I address in this chapter on biocontainment as a form of governance enacted at the level of the organism. It has the consequence of shutting down other debates related to risks, values, or ramifications of synthetic biology and xenobiology. As Ben Hurlbut (2015: 12) puts it, "If risk could be contained within the laboratory and the manipulated organisms, why should the wider public have any say?" This is the result of what I term a sociotechnical imaginary of controllable emergence, according to which, by controlling a biological system (an organism), responsibility can be coupled with design and lead to the management of public opinion. That is, earning public trust and acceptance. It channels that domination of biological systems can be achieved, and displaying safety is instrumentalised to earn legitimation. Biocontainment provides an illusion of safety that if were 100% reliable, there would be no need for other mechanisms for governance.

A major theme I address in this chapter is the imagination of risk that biocontainment suggests. Just as research in xenobiology involves that scientists imagine that life could be different, through biocontainment technologies scientists imagine that full safety can be achieved. The hubris of dealing with safety in biotechnology could lead to reckless behaviour or lead into actions that would not be pursued if safety was not taken for granted. Overconfidence and a misunderstanding of possible negative consequences does not only extend to the realm of technology, but to social relations as well: hubris has led governments into wars that could not have been won, and the illusion of safety that helmets provide prompts more aggressive contact in sports like American football. I bring attention to the performative aspect of the vocabulary of xenobiology to refer to biosafety, because the language scientists use strengthens the association of xenobiology and safety and crystallizes a narrow framing of risk and what is at stake in biotechnology. Such framing of risk runs the peril of ignoring external factors, or 'misuse,' and the consequences of unknown hazards. Biocontainment technologies impair our disposition to maintain our eyes open to what could go wrong.

Biocontainment, or built-in safety, has the potential to lock down matters of governance that could be dealt by institutions, regulation, and social interactions. A problem in believing that risk can be managed in the laboratory is that as an externality, it tends to shut down debates on other aspects of biotechnology. It is important to see xenobiology not as a consequence of scientific self-governance, but an opportunity to restore the conversation about biotechnology and social order ethical, social, and political aspects that have been ignored along the way. Biocontainment is political because it establishes how organisms should be used, for what purpose, and by whom, restricting their agency. It rules how organisms will perform, according to a preferred vision of what organisms should accomplish. If biocontainment seeks to legitimize the release of genetically modified microorganisms in the environment, this raises additional questions about power, such as what distributions of responsibility come into play when engineered microbes are no longer constrained to laboratories? The release of genetically modified microorganisms is also an effort to bring them from the laboratory to the real world (Latour, 1988b). Biocontainment is co-produced with a particular regulation and a regime of knowledge production, it is a product of how in our age we as humans relate to nature and the artificial. In exploring the narrative of safety in xenobiology, I draw attention to how the same narrative can be used for other purposes, like for the protection of intellectual property. I continue this discussion in the next chapter, in which I argue that biocontainment is framed as a problem to satisfy a public that is fearful of new technologies escaping the laboratory; such compliance is a form of responsibility that deserves examination in depth.

## 6. Containment as responsibility

### 6.1 Introduction

The ways in which researchers imagine the public determine their efforts to develop technologies that society adopts in the future. In order to gain trust and legitimacy and avoid controversy, scientists respond to the needs of a public that is perceived as fearful of new technologies (Marris, 2014). Not only does technology need to be contained, but so does public fear (Jasanoff & Kim, 2009). In this chapter I propose that a strategy for achieving acceptance is associating biocontainment with responsibility and enacting governance by incorporating design principles that are technical challenges. This relates to what I term a sociotechnical imaginary of *controllable emergence*, to suggest that risks and public acceptance can be managed in a technological trajectory, insofar risks are defined and framed in advance, and oriented towards the perceived needs of the public. I propose that xenobiologists aim to portray an image of their discipline as responsible, arguing that xenobiology works as a *'technology of compliance,'* because researchers do not address core governance issues directly (i.e., through democratic and participatory mechanisms), but use design principles to satisfy an imagined perception of what the public cares about. By technology of compliance, I also capture that xenobiology seeks to address a perceived understanding of what problems a technology should solve, and what license a technology requires in order to operate in the world.

The limits that xenobiology shifts or expands are not only biological (**Chapter four**), but also social. In the previous chapter I argued that establishing biocontainment as a worthwhile goal has the effect of shutting down other debates related to risks, values, or ramifications of synthetic biology and xenobiology. Biocontainment also provides an illusion of safety that may deflect a prudent approach to biotechnology. Whereas previous chapters have been concerned with biocontainment as a problem of design, and the tension between an unsafe nature and a safer second nature, in this chapter I focus on how scientists perceive society and guide their research activities based on particular framings of previous controversies (i.e., genetically modified crops in Europe) and imaginations of the public. I suggest that scientists draw on folk theories (Rip, 2006b), or particular understanding of a conflict between science and society that lacks a robust empirical basis.

The outline of this chapter is as follows. I first consider (**section 6.2.1**) that there is no agreement in the synthetic biology community about the need for biocontainment of genetically modified organisms, because such organisms have not presented known risks for

the environment or health. Scientists argue that the problem is that engineered microorganisms hardly survive in the wild. I analyse the contested nature of biocontainment as a scientific problem or a problem of risk management. Understanding that the safety (or hazards) of genetic engineering cannot be established as a fact provides context for the ensuing discussion. Subsequently in **section 6.2.2** I explain that biosafety and the risks of genetic engineering are also a public concern whose reach extend beyond the walls of the laboratory. The nature of the debate in the public sphere largely determines the framing of the problem and the solutions available to address it. Next, I show in **section 6.2.3** that the scientists I studied imagine the public as fearful of new technology, thinking that safe-by-design technologies may appease such fears; scientists fear the rejection of the technologies they develop, and it is in their best interest that they are well received by society. Scientists aim to show to the public that they control xenobiology when they plan to use it outside the laboratory; containing engineered microorganisms is also containing public fear. This reflects an imaginary of *controllable emergence*, in which built-in-safety features serve to control engineered microorganisms and their acceptance in society.

In the second part of this chapter, I focus on biocontainment as a form of responsibility. I explain in **section 6.3.1** that synthetic biologists aim to position their field as responsible, and that their understanding of responsibility is consequentialist: by controlling the outcomes of xenobiology, they are acting responsibly. Subsequently in **section 6.3.2** I refer the choice of the principal investigator of the laboratory I studied of not developing an ‘XNA metabolism’ —a mechanism to allow cells to ‘recycle’ XNAs— to highlight that biocontainment involved an ethical commitment. Afterwards I show that control of engineered organisms also derives in other motivations like built-in protection of intellectual property, which must be considered when a narrow focus on mitigation of risk is employed by stakeholders. This point is made clear by referring to the case of ‘Genetic Use Restriction Technologies’ seeds in genetically modified crops, from which I draw lessons for xenobiology.

## **6.2 The public face of biocontainment**

### **6.2.1 Scientists do not agree on the need for biocontainment**

Solutions for the problem of safety or risk in genetic engineering through biocontainment rely on their articulation as scientific problem. Offering responsible solutions depends on how scientists understand and articulate a problem that is influenced by their understanding of other actors. It is not yet settled whether genetically modified organisms are harmful for the environment or for human health, but scientists have tried to close the discussion with

the best scientific evidence available (cf. National Academies of Sciences, Engineering, and Medicine, 2016; National Research Council, 2004).<sup>136</sup> In terms of environmental consequences, controversies have erupted, for example after traces of GM corn was found in wild native corn species (Quist & Chapela, 2001; cf. Sarewitz, 2004). Debates over genetically modified organisms (and particularly crops) are not exclusively about scientific facts and risks, but democratic values, ethics, ways of ordering society, cultural attachment to land and food production (Jasanoff, 2005b). Emerging technologies in our current knowledge production regime require legitimation and public acceptance. If scientists aim to position xenobiology as a solution for the perceived problem of biosafety, it is important to first clarify whether scientists consider that such a problem exists in the first place.<sup>137</sup> Few scientists I spoke to genuinely thought that genetically modified microorganisms were a hazard for the environment, but nevertheless acknowledged that there are uncertainties associated with their uses. Commenting on an article about ‘genetic safety switches’ (Chan et al., 2015), biomedical engineer Karmella Haynes (2016: 56) wrote the following for *Nature Chemical Biology*:

Currently, it is unclear whether the unmonitored release of every genetically engineered microbe (GEM) into the environment is absolutely harmful or absolutely safe. Decades of scientific research and changes in government policies may be needed to determine and define the danger or safety of every type of GEM, as current information is sparse.

Her comment, intended to introduce the subject of biological containment in her piece, draws attention to the risks of the release of genetically modified microorganisms as a problem of *knowing*. Not only is it necessary to question whether genetically modified microorganisms pose problems for the environment, these problems must be identified and knowable to be relevant. Whereas Haynes points out the lack of consensus in the scientific community on whether ‘GEMs’ are safe, scientists have deployed a variety of arguments to call into question the hazards of genetic engineering. Scientific and policy conversations on the subject have matured (to a standstill) over the years since the early debates of the 1970s (see previous chapter; cf. Wright, 1994). If scientists are not fully convinced that biocontainment is a necessity, then why develop built-in safety features? As I explain in this chapter, as a form of *compliance* to a perceived public concern.

Some scientists have questioned the need for biological containment by pointing out the lack of accidents or problems with genetically modified organisms since the dawn of genetic engineering, a period encompassing over forty years. For example, xenobiology

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<sup>136</sup> Nobel prize laureates have joined efforts to claim that GMOs are safe. In June 2016, 108 Nobel prize winners signed an open letter against *Greenpeace* for campaigning against genetically modified crops, especially *Golden Rice*. See [http://supportprecisionagriculture.org/nobel-laureate-gmo-letter\\_rjr.html](http://supportprecisionagriculture.org/nobel-laureate-gmo-letter_rjr.html) [last visited January 31, 2018].

<sup>137</sup> The question of whether GMOs have caused accidents deserves a distinction between microorganisms and crops (plants). I focus in this thesis on microorganisms.

spokespersons Schmidt & de Lorenzo (2012: 2200) write, “That no engineered microbe has even been traced to any disease or has caused any detectable problem is an indicator that safety measures have so far been sufficient (or that forensic methods to this end have worked poorly.” In another publication, the same authors assert that it “appeared that even in the worst case scenario, the safety risks associated with modified microorganisms were not worse than naturally occurring counterparts.” (Schmidt & de Lorenzo, 2016: 90). Scientists display confidence that work with genetically modified microorganisms in laboratories and factories has proceeded with caution and following safe principles.<sup>138</sup> For example, synthetic biologist 17A commented that,

We have huge facilities now dealing with microorganisms producing stuff for us, in huge amounts. We have huge factories, huge bio factories, and we don't see any problems with that. So, we don't see any spill over of microorganisms outside of these factories that are contaminating the environment and creating any kind of problem. So, in a sense, in my eyes, it's like *creating safety valves of something that doesn't require any safety valves* (Emphasis added).

However, the lack of accidents may have been the result of cautious measures taken when GM microorganisms are used in factories or laboratories, without releasing them into the environment. Claire Marris and Catherine Jefferson (2013: 21) point out a well-known epistemological flaw, noting that “*absence of evidence of harm is not the same as the evidence of absence of harm*” (Emphasis original).<sup>139</sup> They also question whether health-related problems associated with GM microorganisms have been properly studied and monitored.

Not only do scientists claim that risks have not been identified but point out reasons why working with genetically modified organisms is challenging. The ‘fitness’ of genetically modified microorganisms has played an important role in safety considerations. Fitness in biology consists of the ability to survive and reproduce in a given habitat. For synthetic biologists, engineered microorganisms are less suited to survive than their natural counterparts. The result of modifications of their genetic constitution that microorganisms undergo renders them *weak*. A complementary idea is supported by interviewee 12A, who in line with the tendency to understand biology in terms of evolutionary histories (**Chapter four**), claims: “The vast majority of engineered bacteria or engineered yeast will not do as well as the natural version does. Because the natural versions... you know... *they evolved*, to be able to work in those natural conditions” (Emphasis added). In the case of xenobiology, XNAs can result toxic for bacteria, making their growth and survival difficult. An interviewee explained that the synthetic organism that Floyd Romesberg and his team developed in 2014 needed a transporter to move XNAs inside the cells (Malyshev et al.,

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<sup>138</sup> Scientists have argued that in factories, biocontainment measures are required to protect engineered bacteria from viruses (Mandell et al., 2015; Rovner et al., 2015).

<sup>139</sup> This is well known fallacy in informal logic, also known as ‘argument from ignorance’. It assumes that something is true because it has not yet been proved false.



2014), which makes the cells weaker. The complex molecular machineries to express and sustain XNAs inside cells that xenobiologists develop impose restrictions on fitness on synthetic organisms. As 14A expressed: “There is no advantage [for the cell] to having any component of the system that we have, and so in that way is naturally contained.” In positioning xenobiology as the ‘ultimate safety tool’ (Schmidt, 2010), the limitations of engineered microorganisms are downplayed, favouring the rationale behind the impairment of transmission of genetic information as the definitive property of safety.

Scientists articulate arguments for and against GM microorganisms depending on the context and purpose. For Victor de Lorenzo, the lack of fitness of GM microorganisms is not only an argument in their favour, but also represents a challenge if such microorganisms are used for applications that require release to open environments. In an interview (publicly available) for SynBioSAFE,<sup>140</sup> after clarifying that laboratory-based bacteria are weaker than their counterparts, de Lorenzo comments:

The problem is not so much that when you put a new bacterium in a site, then this bacteria will start taking over all the existing biological community there. But just the contrary, the very problem is to have the new bacteria being inserted, being colonizing the site that is the subject of our action. So, I don’t see that as a problem, *I see that as a challenge precisely* (Emphasis added).

Beyond the question of the survival of genetically modified microorganisms in the wild, there is the question of whether this is a *scientific concern*. The safety of genetically modified organisms is not a matter of gaining knowledge (since lack of risk cannot be fully proven), but of guidelines and boundaries that must be negotiated. A case in point is an episode that took place in a synthetic biology conference at the *Institut des Hautes Études Scientifiques* in France. After a session that consisted of a conversation between Philippe Marlière and Piet Herdewijn,<sup>141</sup> in the Q&A section a scientist in the audience asked Philippe Marlière the following:

So, you said something about once you get to a certain point, you have to contain things, iron clad way. But it wasn't clear to me, if you select for something that has a gain of function that outperforms wild type, and you can do that for a long time, but almost every time you do that and you test under some other fitness condition, it never can compete with the wild type. So, *is this really a problem?* (Emphasis added).

This comment highlights the contested nature of biocontainment as a problem, somewhere between a scientific question and a question about risk assessment. For scientists, biocontainment may not seem a scientific problem that needs solving. Seen in terms of risk

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<sup>140</sup> See footnote 61.

<sup>141</sup> Discussion between Philippe Marlière & Piet Herdewijn in the Conference on Cellular and Molecular Biotechnology, held in the *Institut des Hautes Études Scientifiques* (IHÉS) in Paris, in December 2015. Available in YouTube: <https://www.youtube.com/watch?v=jlsCIFg8MLY&index=10&list=PLx5f8leIFRgFTshIFyIWDpkag0C2StIma&t=0s> (minute 27:43 of the recording) [last visited January 11, 2018].

management, or scientific governance, the picture is different. Questioning the fitness of genetically modified organisms is important if scientists promote biocontainment as an opportunity to justify the release of such organisms to the environment. Occasions in which the topic of safety-by-containment is debated in public reflect a tension in terms of who has the authority to define whether a problem is worth solving, and the nature of the problem; whether there is a solution (biocontainment) that needs a problem, or a solution is needed for a genuine problem. In this sense, the question becomes who has the authority to frame an issue as a hazard, or a technology as safe, and for what purposes these conceptions are mobilized.

If scientists are not convinced that biocontainment is necessary, why do they consider it worthwhile? They propose that synthetic organisms are different from previous advances in genetic engineering, therefore they present unknown challenges, or impacts that are difficult to predict. Synthetic biology faces the question of how much distance it should take from previous approaches in the life sciences like as genetic engineering of crops, in order to avoid associations with past controversies. Hence the need to provide an impression that risks are being considered. Dana and colleagues (2012: 29) write in their essay on managing risks in synthetic biology

Unlike transgenic crops, synthetic microbes will be altered in more sophisticated and fundamental ways (such as elimination of metabolic pathways), making them potentially more difficult to regulate, manage and monitor. They might also have environmental impacts that are difficult to predict.

Synthetic biology seeks being associated with safety and responsibility (Torgersen, 2009); indeed, avoiding a GM controversy is high on the agenda for scientists, such as Sven Panke, as he explains in the SynBiosafe interviews.<sup>142</sup> This is a problem that is social, there is not one solution and it is questionable if it is a problem at all. What it suggests is a linearity in thinking about science in society, establishing that science should continue to advance in a trajectory of growth, decoupled from public opinion. This not only suggests an understanding of previous 'controversies' or disputes, but dictate the conditions for future controversies, because the roots of social discomfort with science and technology is not properly identified. In the next section I show that the safety of xenobiology and synthetic biology are a matter of public opinion and how scientists understand the needs and concerns of other actors.

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<sup>142</sup> See footnote 61.

### 6.2.2 Biocontainment as public concern

It is time to bring the public into the discussion of the nature of the problem that biocontainment represents. The tension between the risk of genetically modified organisms as a scientific question or a risk assessment question extends to debates that involve the public; questions about safety of genetic engineering are a problem of public policy and knowledge in public arenas. A case in point is the newspaper article *Scientists are actually creating microscopic life in laboratories. Should you worry?*<sup>143</sup> that reported on two scientific articles on xenobiology published in early 2015.<sup>144</sup> The author writes “let’s cut to a basic question: Are GMOs safe? Nothing controversial there! Seriously, you can answer this question round or square *depending on which experts and activists you contact*” (emphasis added). Noteworthy, the author requested comments from synthetic biologist Steven Benner (via e-mail). Benner replied that genetically modified organisms are not fit for surviving in the wild, providing an explanation supported by evolutionary biology, and clarifying that the question is different for GM plants. Benner turn around the question from a scientific matter to a question about risk, as a problem of public knowledge and decision making. He emailed the following to the author’s article:

The American body politic has difficulty understanding risk. In fact, by any standard of risk, genetically modified organisms pose no risk at all. These two papers begin by denying this fact. Thus, their difficult technological work has no purpose.

Benner questions the purpose of research in biocontainment, and downplays the scientific achievements as unnecessary, as the product of an incorrect understanding of risk by the American public. In doing so, he conveys that questions about containment in xenobiology are questions of science and social order. Benner also draws attention to how giving space in the media to such research draws attention to what he perceives to be a non-existing problem and confuses its management:

On the contrary, by asserting in a prominent place (the journal *Nature*) that this non-existent risk needs solution, these papers subtract from the *ability of the body politic to do sensible risk assessment to create sensible public policy*.

Benner does boundary work to keep questions about the risks of genetic engineering as a problem that only scientists can determine. Biocontainment, as a question of *public policy*, is meant to be dealt with scientific knowledge. This has been noted before, related to discussions about the Asilomar conference. Ben Hurlbut (2017: 80) writes, “In 1976, Senator Edward Kennedy (D-MA) criticized the Asilomar scientists for appropriating the authority

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<sup>143</sup> Achenbach, J. Scientists are actually creating microscopic life in laboratories. Should you worry? January 27, 2015. The Washington Post. <https://www.washingtonpost.com/news/energy-environment/wp/2015/01/27/scientists-are-actually-creating-microscopic-life-in-laboratories-should-you-worry/> [last visited October 19, 2017].

<sup>144</sup> See Mandell et al., 2015; Rovner et al., 2015. These articles have received wide press coverage due to the relevance of their findings. See also **Appendix one**.

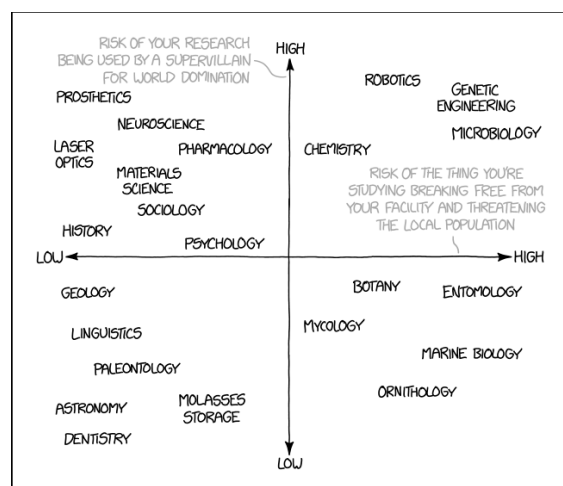
to govern: ‘they were making public policy, and they were making it in private’” (quoted in Culliton, 1975: 1188). Containment brings together science and governance in a way that is difficult for actors like Benner to keep separate or purified. Moreover, Benner suggests that decision-makers should question the appropriateness of the technology, not technological design:

Public policy still needs to recognize the impact of technology ...

[and in a separate paragraph]

However, here, policy prescriptions must reflect social values and goals; *they have nothing to do whether the technology used to achieve these involves recombinant DNA genetic modification, or classical tools for genetic modification* (emphasis added).

Benner’s ideas are in line with other scientists referred in this section who consider biocontainment a technological problem. The public is fearful of genetically modified organisms stepping out of the laboratory, constituting a fundamental imaginary of Western societies. The following cartoon (**Figure 10**) from the webcomic XKCD.com<sup>145</sup> illustrates stereotypes over two concerns for emerging technologies. The first is dual use, or biosecurity, which has been a long-standing concern in debates over biotechnology and society (Evans, 2016). Commentators of synthetic biology fear that manipulating life may become easily accessible and cheap, which may lead to actors with bad intentions, like terrorists, to commit harm using biological tools. Xenobiologists have tried to set distance from these concerns, claiming that serious hazards of misuse can occur with DNA, for example with the modification of viruses known to affect humans. Nevertheless, the fiction of a ‘supervillain’ using bioweapons to advance his interests has been entertained in many films and the popular imagination.



<sup>145</sup> XKCD.com website is described in its website as a “A webcomic of romance, sarcasm, math, and language.” It is produced by physicist Randall Munroe. See [www.xkcd.com](http://www.xkcd.com). In the Wikipedia entry on the subject, the subject matter of the comic is described as varied as “statements on life and love to mathematical, programming, and scientific in-jokes. Some strips feature simple humor or pop-culture references.”

Figure 10 Comic titled 'Research Risks.' Source: XKCD, a webcomic run by Randall Munroe. From <https://m.xkcd.com/1904/> [last visited November 1, 2017].

The horizontal axis of the cartoon represents concern about the escape of a technology from a genetic engineering 'facility.' In my interpretation, this depiction portrays a laboratory that is kept in secrecy from the local population, where the military conducts suspect research; this is for example the plot of the recently acclaimed TV show *Stranger Things*. This reflects the view that research can take place in contained spaces like a laboratory without the need for justification. It is when the products of research trespass the physical and imaginary barrier of the laboratory and the real world that hazards are contemplated as real. Genetic engineering and Microbiology are depicted as both with a high risk of being misused by villains and escaping a 'facility' and threatening the local population. This context generates a need for scientists to *justify research* in their field, to make it seem developed in a responsible manner. Scientists face the task of dealing with perceived threats of emerging technologies and keeping their laboratory's lights on.

To gain a richer picture of why biocontainment is an aspiration of xenobiology it is important to analyse how the safety of genetic engineering is portrayed in public settings. The release of genetically modified organisms is a hotly debated topic in many settings, like public dialogues and discussions. More than the release of organisms, concern is rather about whether scientists can control their 'creations,' and whether a lack of control can affect human populations in negative ways.<sup>146</sup> Concerns over the release of genetically engineered microorganisms were frequently raised in the public interviews and panel discussions that I analysed. A common theme was an interviewer being asked about their research projects, or a high-profile study. For example, the interviewer asked synthetic biologist Jef Boeke from NYU in an interview for *Live Science*, "What types of safeguards to protect the public are used in laboratories where research in synthetic biology is conducted?"<sup>147</sup> In an interview for *Chemistry Views* with Caltech protein engineer Frances Arnold, the interviewer asks her, "How can you make sure you are not creating *something that will get out of control?*"<sup>148</sup> (emphasis added). Control in this context could refer to ensuring that new creations in the laboratory will not put in danger human populations in danger. Are researchers in control because of their capacity to create rather than what they create? Furthermore, in an interview

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<sup>146</sup> The story of *Frankenstein* by Mary provides a good reference to think about control and responsibility. For Bruno Latour, the fault of young scientist Victor Frankenstein was not to care enough about his creation, not support its entrance to the world (Latour, 2012).

<sup>147</sup> Interview to Jef D. Boeke, by Lily Whiteman. <http://www.livescience.com/19264-understanding-synthetic-biology-boeke-nsf-bts.html>

<sup>148</sup> Interview to Frances Arnold, by Vera Köster, [http://www.chemistryviews.org/details/ezone/1376211/Interview\\_with\\_Frances\\_H\\_\\_Arnold\\_\\_Design\\_by\\_Evolution.html](http://www.chemistryviews.org/details/ezone/1376211/Interview_with_Frances_H__Arnold__Design_by_Evolution.html)

for CBC Radio the interviewer asked synthetic biologist Floyd Romesberg “what happens if the organisms with artificial DNA get out freely into the world and start interacting with other organisms that only have natural DNA?”<sup>149</sup> The subject of release also came to the surface in public dialogues, oriented toward gaining a glance of public attitudes toward new technologies. For example, in the public dialogue that the BBSRC requested in 2010, a participant expressed:

If it can be confined it sounds safer. I just think if you can box it, it just feels that much more safe. The minute you release it out there you just have no control, as much control you want to have, you don't, because you're in a natural environment.<sup>150</sup>

It should not be surprising to find concern among ordinary people about new technologies emerging out of laboratories, which reflects an instinct of maintaining boundaries over what we perceive as potential hazards. Our ancestors conceived nature or the wilderness as what is found beyond the boundaries of cities. Humans have built walls through history to protect themselves from enemy invasions, building walls in cities, and landscapes, like Hadrian's wall, the Chinese Great Wall, or Donald Trump's proposed border wall with Mexico. This relates to hardwired perspective of dealing with threats that extends to the technological realm. Nuclear disasters like Fukushima and Chernobyl were 'contained' by covering them with a block of concrete. Moreover, the connection between containment and release is displayed in popular culture. For example, the television show *West World* features a 'Wild West' type of theme park in which robots act and look like humans and visitors are allowed to dwell in their fantasies and enrol in different adventures. To contain the agency of the robots which have dreams of their own and may desire to escape the park, the creators of the park built an explosive device inside them that activates in case they escape outside the boundaries of the park. In this way, the design resembled a form of built-in safety, which in the show, the robots are able to dismantle in their quest for freedom from their creators. In the next section I show that such stereotypes and ways of imagining the public translate into design principles, like built-in-safety, which aim to gain public trust. As I show, such perception of a fearful public have emerged in combination with technological progress over the last decades, including depictions in the media and popular culture. By addressing such perception, scientists are not contributing to having a profound conversation about what is at stake and the type of society that technological progress conditions.

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<sup>149</sup> Radio show 'The Current' by Ana Maria Tremonti, in CBC, May 21, 2014. Interview to Floyd Romesberg and Jim Thomas (comment from Romesberg). See <http://www.cbc.ca/radio/thecurrent/may-21-2014-1.2908110/expanding-the-alphabet-of-life-with-artificial-dna-1.2908115> [last visited 04 April 2017].

<sup>150</sup> Biotechnology and Biological Sciences Research Council Public Dialogue, 2010: p. 58. Retrieved from <http://www.bbsrc.ac.uk/engagement/dialogue/activities/synthetic-biology/findings-recommendations/> [last visited 04 April 2017]

### 6.2.3 Built-in safety will satisfy ‘all these people’

Biocontainment serves not only to render GEMs safe but to protect them (and scientists) from public scrutiny. Synthetic biologist George Church refers to this link between a perceived problem of public fear and genetic engineering as a question of moving forward by designing safety features. In an interview for *New Scientist*,<sup>151</sup> Church commented that “[w]hat critics of GMOs want is something where GM stays isolated... That’s why we wanted to embed these safety features, to show the bacteria can’t escape.” He raises a common theme in this thesis, adding the question of what types of publics resist to genetic engineering, including ‘critics of GM,’ usually found in civil society and activist organizations. The actors I analysed do not make a fine-grained distinction between the multiple publics that co-exist, ignoring their heterogeneity. Nevertheless, despite the undefined character of public(s), the role of critics and civil society organisations in innovation processes is multi-faceted (Ahrweiler et al., 2018) and plays a role in co-producing the narrative of biosafety through biocontainment that I studied.

Recently, Ian Sample, the science editor of *The Guardian*, warned that “artificial intelligence risks GM-style public backlash.”<sup>152</sup> Judging by the title, the article appears to suggest that an emerging technology, like artificial intelligence, needs protection from public backlash to continue its advancement. The article did not cover in depth the origins or manifestations of public criticism of genetic engineering, building on a widely agreed narrative—a narrative that suggests that ‘GMOs’ are bad but without a thorough historical basis. The article quotes researchers from Imperial College London, who comment that artificial intelligence “could lead to societal backlash, not dissimilar to that seen with genetically modified food, should serious accidents occur, or *processes become out of control*” (emphasis added). This highlights the importance of *controlling* the technology. Not only the technology needs to be controlled but also its diffusion in society. In my data I noted that avoiding a GM-style controversy is an important consideration for researchers in synthetic biology. For example, Sven Panke<sup>153</sup> comments in an interview for SynBioSAFE:

We have to realize that the first wave of genetic engineering, end of the 80s, early 90s, here in Europe, led to a number of rather unfortunate communication problems. People are afraid

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<sup>151</sup> Regarding Church’s lab groundbreaking publication in xenobiology (Mandell et al., 2015). Quote extracted from Coghlan, A. Lab-bound bacteria could lead to ‘safer’ GM organisms. *New Scientist*. 22 January 2015. Retrieved from <https://www.newscientist.com/article/dn26835-lab-bound-bacteria-could-lead-to-safer-gm-organisms/> [Last visited November 3, 2017].

<sup>152</sup> Sample, I. Artificial intelligence risks GM-style public backlash, experts warn. *The Guardian*. 1 November 2017. <https://www.theguardian.com/science/2017/nov/01/artificial-intelligence-risks-gm-style-public-backlash-experts-warn> [last visited November 2, 2017].

<sup>153</sup> SynBioSAFE interviews; see footnote 61.

of what people do, of what scientists do. ... it would be great if we could prevent a similar development for synthetic biology.

For Gautam Mukunda,<sup>154</sup> a graduate student in political science, the risk of synthetic biology is that the field may not realize its promises: “The biggest short-term risk is in synthetic biology is that the technology won’t happen. *The biggest short-term risk is that people stop it*, that people get scared by this idea of us creating life” (emphasis added). For xenobiology and its promise of containment, safety-by-design can be seen as a strategy to ‘protect’ the technology from the public, while conveying the notion that it seeks to protect the public from the technology.

Nevertheless, I found that synthetic biologists do not have a complete picture of the causes of the genetically modified food controversy in the 1990s. Its unfolding contributes to ‘folk theories’ (Arie Rip, 2006b) that associate controversies over technology with lack of ‘safety’ in GM organisms. Scientists draw on explanations of their own making to account for the perceived imagination of a public resistant to emerging technologies. As a result of the impression that the public fear new technologies, scientists adapt the claims they make about xenobiology to brand the field as a safe discipline. It is expected that people would be afraid of innovation, but once the benefits are seen, and risks shown to be negligible, then people would come to accept it. For example, Víctor de Lorenzo remarks<sup>155</sup> that “every time a new technology appears in society, and this technology is likely to have an impact in our lives, there is a reaction in which fascination with the new technology is combined with fear.” For 16B, if the public knew about the science behind innovation, they would appreciate new technology. Some researchers in xenobiology hold the view that fear about the perils of synthetic biology is not well grounded nor justified. According to them, the field is not so ‘scary,’ and if the public *understood the science*, they would not be fearful. For example, interviewee 14A comments that:

There is this general misunderstanding that this kind of change could spread out into the world. ... If our *E. coli* were to escape into the real world, they would never survive. I think that's the thing that people don't understand.

After explaining that the strains are not pathogenic and have low probability of surviving outside a laboratory, 14A continued,

But I think if you were to explain that concept, people just have this fear of what they think is now alien DNA, sort of a very foreign thing to them and they're naturally inclined to be afraid of it.

Synthetic biologists and xenobiologists promise safety to gain support for their research, confident that decisionmakers and research funders also imagine that the public expects that risks are kept under control for accepting new technologies. Biocontainment then complies

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<sup>154</sup> Ibid.

<sup>155</sup> Ibid.



with the needs of the public. Research in xenobiology is a manifestation of how scientists think science should advance, and how they interpret their relationship with society, that becomes more and more porous as scientists need to permeate the doors of their protected spaces (Rip, 2011). Developing biocontainment works as a performance of compliance, a strategy to satisfy a public that needs to be governed; in this sense, it serves as a form to reach audiences (or publics), establishing a form of communication that scientists can rely on. If there is a perceived rule –ensuring that technologies are safe and controlled– then it is better to follow it than opening discussions over what safety and control mean. For instance, interviewee 19A expressed:

They're [scientists] aware of the need for that [biosafety] because of legislation, because of what the public might think, and also nongovernmental organisations who maybe wanting to lobby against the kind of technology. So, unless we are deliberately designing all these safety features in, right from the start, then *we'll not be able to satisfy all these people* (emphasis added).

Governance and public acceptance are dealt with by incorporating safety features, more than with other institutional and democratic mechanisms. The introduction for a major study in xenobiology by George Church's laboratory reads, reflecting the intertwining between biocontainment, the release of genetically modified organisms, and public concerns:

GMOs are rapidly being deployed for large-scale use in bioremediation, agriculture, bioenergy and therapeutics. In order to protect natural ecosystems and *address public concern* it is critical that the scientific community implements robust biocontainment mechanisms to prevent unintended proliferation of GMOs (emphasis added) (Mandell et al., 2015: 55).

Scientists frame biosafety as a scientific question when it is also a public policy question, as explained above. For example, referring to xenobiology, Victor de Lorenzo (2011: 5) writes that “The possibility of having live cells without familiar genetic material that can evolve, mutate or pass on to other recipients would certainly *resolve many of the hypothetical dangers that (true or invented) afflict synthetic biology in the public imaginarium*” (emphasis added). Scientists in their hubris over technological solutions may ignore other mechanisms for governance that could help better achieve the introduction of new technologies in society in ways that are beneficial for all. Hence, biocontainment also serves to signal a boundary not only between the laboratory and the real world, or between the natural and the unnatural, but between publics and scientists. It is possible that scientists want to hold on to the comfort of letting science speak for governance more than dipping into the messy dynamics that come with politics and deliberation about technology. Establishing a direct connection between the problem (public fear that will block potential innovations which will yield benefits for all) and the technological solution (organisms with alternative genetic systems) makes it difficult to have important conversations about the deployment of new technologies in society and how these affect social fabrics, transforming the world in profound ways. Simply put, if the solution to a problem is so simple, it becomes a matter of advancing the technology forward,

without having to question the motivations behind the research. By imagining a fearful public whose trust can be earned by developing built-in-safety features, scientists may face consequences by not grasping the complexities and nuances of science in society, privileging their own worldview of how scientific matters and technologies should diffuse into society.

#### 6.2.4 A shared understanding of safety

In what follows I suggest that other stakeholders like public servants and regulators share with scientists the view that the future of emerging biotechnologies depends on a fearful public that requires safety, and biosafety can be addressed with design principles.<sup>156</sup> In my interpretation, for regulators, containment technologies provide a mechanism to regulate a field and permitting its advancement, it is a win-win situation. Public acceptance and regulation become barriers that may constrain the advancement of xenobiology, corroborating that the field is not only limited by what is biologically possible, but by what is socially and politically acceptable. Containment serves to navigate such limits. Interviewee 26A supported this view, saying that “there are no limitations what could be done. But there will be also regulatory limitations which might control scientific evolutions.” Synthetic biologist 12A commented to have worked frequently with regulators in order to commercialize one of the technologies developed in their laboratory. According to 12A, it is not convenient for regulators to impose roadblocks to the advancement of innovation. When asked about the possibilities that releasing organisms would enable, 12A commented that “those are not scientific decisions, that’s just political considerations.” 12A also explained that there is not a strong reason for not releasing microorganisms into open environments, clarifying that

Except for regulators saying we don’t want that. By building new xenobiologies, auxotrophies, kill switches, these things just help; they may, they may not, but they effectively just answer the questions that the regulators might want to have an answer before they leave something like this go out.

Regulatory agencies and their guidelines face a difficult position to navigate because they need to find a balance between promoting innovation and ensuring that innovations are ‘safe’ (Jasanoff, 1997). The regulation of synthetic biology undergoes a difficult process in which institutions that manage risk need to keep up with new developments. Containment in xenobiology can be seen as a strategy to embed forms of regulation in the organisms themselves. Matters of regulation and funding reinforce each other. Scientists develop safety features to satisfy the public and regulators, while regulators want technologies to be

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<sup>156</sup> This section is based on secondary data and the impressions of scientists about views of actors like policymakers and regulators See **Chapter four** for details.

developed safely, often with technical solutions. Hence a technology that promises safety appeals to both.

The principal investigator of the laboratory I studied explained in a group meeting that two grants that his laboratory had were associated with biosafety, suggesting that biosafety had been important for securing these grants. These grants were awarded by European funding bodies with a mission to promote the development of synthetic biology. The importance of safety in genetic engineering as a strategic focus is evident in different grant calls. For example, the project PreSto GMO-ERA-Net (<http://www.presto-gmo-era-net.eu>) intended to evaluate “GM organisms intentionally released into the environment and/or used immediately in feed and food applications,” which would lead to the implementation of an EU wide research network (GMO ERA-Net) to study the acceptance of ‘green biotechnology’ in Europe. Other European agencies, like the BBSRC and the European Commission, have provided funding for projects related to biocontainment. An important consortium for the support of synthetic biology, ERASynBio,<sup>157</sup> has also financed projects related to biosafety.<sup>158</sup> Its report *Next steps for European synthetic biology: a strategic vision from ERASynBio* (ERASynBio, 2014) cited the study about chloro-uracil supporting *E. coli* conducted by Philippe Marlière and colleagues (2011), as an effective safety alternative. Moreover, the report of the ERASynBio ‘1st Strategic Conference’ displays several roadmaps that depict biosafety as a relevant feature of the next steps in synthetic biology.<sup>159</sup> **Figure 11** shows a roadmap that displays a variety of technologies required for synthetic biology. The same figure only includes three technologies for the ‘long term (2025+)’ (top right), two of which are related to xenobiology: ‘safe by design technology,’ and ‘synthesis of non-DNA based life.’

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<sup>157</sup> See footnote 54.

<sup>158</sup> See <https://www.erasynbio.eu/joint-calls> [last visited November 4, 2017]. See also ERASynBio, 3rd Joint Call. Retrieved from <https://www.erasynbio.eu/joint-calls/3rd-call> [last visited August 3, 2018].

<sup>159</sup> See [www.erasynbio.eu/lw\\_resource/datapool/items/item\\_69/erasynbio\\_1st\\_strategic\\_conference\\_roadmaps.pdf](http://www.erasynbio.eu/lw_resource/datapool/items/item_69/erasynbio_1st_strategic_conference_roadmaps.pdf) [last visited July 18, 2017].

Important underpinning technologies for synthetic biology			
Current (2013)	Short term (2014-2018)	Medium (2019-2025)	Long term (2025+)
Systems engineering	Metrology metrics	Synthetic biosis	Safe by design technology
Bioinformatics for systems engineering	3D, parallelization and miniaturization of experiments	Synthesis of non-DNA based life	
Well controlled bioreactors	Automation	Re-scale up	Digital organisms
Well defined chassis organisms	Web based Information Systems		
Sequencing	In-vivo assembly		
DNA synthesis	Professional registries		
Quantitative characterization	Good model repositories		
Heterogeneity & noise / single cell analysis	Design tools predictive		
Better Systems Biology definition of parts	Common standards with Systems biology		
Well defined Systems Biology chassis	Capacity to handle? Circuits: Systems Biology		

Figure 11. Important underpinning technologies for synthetic biology. Source: ERASynBio 1<sup>st</sup> strategic conference roadmaps.

If risk can be embedded in a technology, funding agencies and regulatory agencies both gain as they fulfil their mission of promoting innovation and ensuring that innovation is safe. Biocontainment becomes a metaphor for talking about the diffusion of novel technologies in society in a context in which society has become less trustful of scientific institutions. As such, containment can be seen as a strategy to preserve the authority of science for defining what constitutes a problem, and how it should be addressed. It keeps conflicting worldviews over the use of GMOs in the arena of science, grounded on the persuasive power of facts to establish appropriate decision-making. This explains framing biosafety in scientific terms, manageable and quantifiable via the properties embedded in manipulated organisms. In the second part of this chapter I extend on scientific practice and responsibility in xenobiology. To consider responsibility in science as the compliance to a set of perceived needs from the public and regulators about controlling the risks of a technology, it is necessary to understand how the problem of safety and risk in genetic engineering is articulated by various actors; how we define and understand a problem defines the type of solutions based in science to address it.

## 6.3 Responsibility and control

### 6.3.1 An image of responsibility

Synthetic biology has gained attention for incorporating an ‘ethos’ that favours open science, entrepreneurship, and access to a larger audience than academic scientists (i.e. DIYbio and iGEM) (See **Chapter two**). Another cultural manifestation is the desire of scientists to portray themselves as ‘responsible’ and stewarding the discipline in a manner that is safe and ethical. In **Chapter one** I introduced a video that the Austrian NGO *Biofaction* made about the first xenobiology conference, in which responsibility is portrayed as a feature of

xenobiology.<sup>160</sup> René von Schomberg, pioneer in responsible research and innovation (RRI), referred to the vision of xenobiology as navigation (**Chapter four**), and commented, “You cannot send a risk assessor on the ship of an explorer, this would jeopardize the exploration ... But you could accompany a ship with an assessor, so maybe you should have two ships.”<sup>161</sup> In this section I explain that scientists and supporters of xenobiology intend to portray an image of being responsible, for which biocontainment is a good strategy to earn trust. Regarding responsibility, we must ask in what terms it is mobilized, and for what ends? Scientists aim to be *perceived as responsible* by conducting responsible science that is safe and aware of the risks that may arise in the search for benefits and capital. Calls for responsibility can be attributed to ethical issues, but these are also ambiguous, or ill-defined. Markus Schmidt commented in an interview for the BioArt Society<sup>162</sup> that “we need to stay ethically vigilant on developments in synthetic biology, observing the developments and be as considerate and responsible as possible. But we also need to discuss again what it is that we want to achieve, what should be off-limits and conserved, and what should be OK to be modified.” Whereas proponents of xenobiology want the field to be associated with responsibility, the quest for responsibility is commonplace in emerging technologies (Jonas, 1984). Ben Hurlbut (2015a) argues that synthetic biology displays a reimagination of responsibility in which scientists are granted the authority to ‘enunciate’ the right challenging societal problems to be solved with technology.

The inclination to frame synthetic biology as a responsible discipline is evident in the report *New Directions: The Ethics of Synthetic Biology and Emerging Technologies* (Presidential Commission for the Study of Bioethical Issues, 2010). This report, commended as a response to the development of a *Mycobacterium* that was transferred to a genome made of synthesized DNA (Gibson et al., 2008), concerns five main points related to sustainability and anticipatory governance (cf. Wiek et al., 2012). The report is ample in scope and makes sensible considerations such as involving the public, stopping research when necessary, revisiting intellectual property, and debating the distribution of benefits. The report attributes biosafety a role in responsibility: “A number of safety features can be incorporated into synthetic organisms to control their spread and life span. Surveillance or containment of synthetic organisms is a concrete way to embrace responsible stewardship.” (Presidential Commission for the Study of Bioethical Issues, 2010: 9). For the Presidential Commission, ‘responsible stewardship’ is an ethical principle that can be supported by biocontainment measures.

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<sup>160</sup> See footnote 8.

<sup>161</sup> Ibid.

<sup>162</sup> See <https://bioartsociety.fi/projects/making-life/posts/interview-synthetic-biology> [last visited November 6, 2017]

Even though synthetic biologists commit to conducting responsible research, responsibility is ambiguously expressed, often associated with safety. For example, professor of Chemistry Scott Mohr from Boston University mentioned in an interview for SynBioSAFE<sup>163</sup> that ‘what I think is beginning to grow in the people in the community is the idea that they must take responsibility.’ Taking responsibility suggests a redefinition of the terms under which scientists conduct science to expand their duties to include being more caring and responsible about their research outputs. Markus Schmidt & Victor de Lorenzo (2012) warn about the potential that scientists possess to stir controversies. They refer to a public controversy motivated by geneticist Jonathan Beckwith regarding the first physical isolation of the DNA segment of a gene that sparked international media coverage and controversy. Warning of a GMO-type controversy, they state that “raising awareness on one’s research topic by playing on the hopes and fears of other people will bring attention on the short term but could turn out to be a boomerang over the long run” (ibid., 2204). Responsibility is framed as a problem not only of safety, but also of communication of sensitive issues. For interviewee 27A, responsibility was a matter of transparency, of the public having access to scientific knowledge. Other interviewees referred to responsibility in a consequentialist sense of being held accountable for events that may happen in the future and were not planned or intended by the researcher.

If containment can be understood as responsible design, it is important to situate the discussion in the context of the discussions with the laboratory. I opened the third group discussion in the weekly laboratory meetings by asking participants about how they would define responsibility in science it. The first reply was the following,

Responsibility is ambiguous. So, if you do something irresponsible, then something goes wrong, then it’s yours to blame. Which I know that is not the meaning that RRI is developing. It’s been developed as consequence. Everything you do has a consequence, so you should be able to think or plan to the consequence before you do what you set yourself to do.

Thinking of consequences also carries the need to limit further blame. Following the quote above, another member of the laboratory commented that “the idea of blame is that something will happen that you haven’t thought of,” which was complemented by an additional comment that “consequence, is better just said, can be conscious or unconscious.” This is in line with a consequentialist perspective on responsibility, according to which moral responsibility is ascribed to the outcomes and results of a technology (Doorn, 2012). The discussion turned to the possibility of knowing and predicting consequences. These ideas are in line with the notion of an XNA metabolism, for which, responsibility is incorporated into the design, and where the researcher aims to tightly control the behaviour of their creations once they are used by others; metabolism in this context refers to developing features so cells

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<sup>163</sup> SynBioSAFE interviews; see footnote 61.

can ‘recycle’ or break down XNA nucleotides (or artificial amino-acids) and incorporate them in other cellular processes, for example to produce energy, or primary metabolites.

As explained above, researchers display being responsible as a way to earn public acceptance of synthetic biology and respond to a perceived potential backlash. As Moe-Behrens and colleagues (2013: 2) write explicitly, to fulfil the potential of the field, responsibility is the key:

If synthetic organisms and their derivatives are to become as ubiquitous as electronic devices, then synthetic biologists must openly address the responsible and safe use of synthetic biological systems. *We can assuage fear and foster familiarity with synthetic biology* through effective efforts to inform the public of the actual risks of synthetic biology research, the steps we can take to address the risks, and how this technology can be harnessed to meet society’s needs (emphasis added).

This quote reflects three considerations about how synthetic biologists conceive responsibility in their discipline. First, the authors believe that the safe use of biological systems can lead to familiarity and acceptance of synthetic biology. Second, they place the centre of gravity of responsibility upon scientists, rather than conveying responsibility as a unified effort between different actors (and especially users). Third, they reflect an underlying theme in RRI of mobilizing technology to meet society’s needs. For scientists, displaying ‘responsibility’ through built-in safety in synthetic biology can play an instrumental role in securing public acceptance that (hopefully) earns public trust. As biocontainment is mobilized as a form of responsibility, this implies that responsibility can be delegated to design principles and subject to what scientists determine it to be. Moreover, developing biocontainment features might be considered as ‘sufficient,’ hampering further efforts that could be necessary for properly govern synthetic biology, including ensuring a right distribution of risks and benefits, as well as deliberation about values reflected by advances in the field. If biocontainment technologies are effective in their goals of separating artificial organisms from natural ones, as some of the goals of xenobiology hold, then there is a chance that discussing questions about ethics or politics are sidestepped. For example, when asked about the ‘key ethical and regulatory issues that must be addressed’ for synthetic biology, Ron Weiss answered (for an article in *Nature*) by changing the subject from ethics to risk:

Like other responsible scientific fields of endeavour, synthetic biology has an ingrained culture of seeking to reduce risks with existing technological solutions, while seeking to predict and avoid problems with proposed new solutions (Church et al., 2014: 293).

Safety is without doubt an important element of responsibility. It hardly makes sense to advocate for genetically modified organisms that are less safe, or less controllable. For example, in a brief for ‘G20 Insights’ about synthetic biology policies, scientists Alexander Kagansky and Bartłomiej Kolodziejczyk recognize that “there are myriads of scientific, social, commercial and legal issues” (Kolodziejczyk & Kagansky, 2017: 1); they suggest ten proposals related to safety and risk management, except for two postulates that call for a

revision of intellectual property frameworks and regulation of Do-It-Yourself biology. But governance is about more than design principles: it incorporates social relations, procedures, compromises, and many other aspects that seem to be obscured by biocontainment technologies.

As a legitimization strategy, associating biocontainment with responsibility may not ensure earning public acceptance. STS scholar David Guston made this point in an interview for *Science Friday*,<sup>164</sup> about George Church's laboratory paper in 2015 (Mandell et al., 2015) (See **Appendix one**). The show's host, Ira Flatow, asked Guston: "While those safeguards may reassure a scientist, will they convince people who are sceptical of genetic engineering that these organisms are truly safe?" Guston replied that genetic safeguards could not work as a "silver bullet for creating vast public confidence around genetic modification and the full agenda of synthetic biology." Noteworthy is not the perceived flaw of biocontainment to earn public trust, but the confidence that scientists might deposit in this possibility. It is not clear for me that scientists recognize that a safety-by-design approach may possess flaws as Guston suggests, an important consideration for thinking about governance in xenobiology. This is understandable if responsibility in xenobiology works as a performance of safety to comply with a set of expectations by a wide array of supporters of the field. Part of the role of STS analysts is to extend bridges between social scientists and life scientists to make these misunderstandings of narratives clear. In other words, delivering the message and enabling rich conversations about the limitations of biocontainment as a mechanism for governance, as well as the opportunities it can present. Moreover, as commentators we should pay attention to what are *not being told* about biocontainment. Is there something hidden in the words of scientists and supporters of synthetic biology? If biocontainment can be understood as a metaphor for solving a friction between and society, it also reflects tension within the scientific community. A friction that favours technological solutions over social arrangements and political devices.

It is useful to think of biosafety and xenobiology as a collectively held imaginary guiding action, according to which, safety —helping gain public acceptance— can be achieved through design principles. Insofar different actors like scientists and decisionmakers share this view, they will agree to mobilize resources and efforts towards what can be perceived as a priority, the development of safer biological systems. Of course, it is not the only priority in the agenda for synthetic biology, but it is an important one. Imagining safety as achievable by design may not translate into discrete objects but reflects a perspective in the governance of the life sciences, that highlights the goal of xenobiology —linked to biocontainment— is as much about ensuring public acceptance as portraying an image that scientists are giving

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<sup>164</sup> See footnote 129.



the right steps in the right direction, so they can maintain their research activities and career advancement. Put otherwise, and relating to the Asilomar conference, is a way for scientists to maintain their authority to establish what issues deserve attention, by showing they are acting in a responsible way.

### 6.3.2 The XNA metabolism: ethics, distribution and control

I have argued that responsibility in xenobiology is articulated by scientists as establishing control over the outcomes of genetically engineered microorganisms. In this section I analyse the decision of the principal investigator of the laboratory for not developing an *XNA metabolism* as a case to reflect upon what responsibility in synthetic biology means. Developing an XNA metabolism reflects that different technologies can follow different paths, the result of contingent historical processes and decisions that researchers make. The choice of not pursuing an XNA metabolism embeds anticipation of risks according to an imagination of what deserves control and attention in genetic engineering. This implies that the principal investigator imagines how his creation could be used and has thought of it as a solution to avoid unintended consequences is restricting its range of operation.

The principal investigator's notion of metabolizing XNA materials draws on ideas proposed earlier by pioneers of xenobiology, in a way that builds on the robustness of biocontainment as a safe approach. Markus Schmidt (2010) listed ten specifications for ensuring safety of XNA-based organisms, including environmental considerations. The second specification addresses the 'XNA metabolism'; Schmidt writes that "Natural organisms must also not be able to produce these essential biochemicals, to avoid a symbiotic relationship with XNA" (ibid., p. 328). This means that XNA must be produced artificially in the laboratory. The laboratory's principal investigator explained to me that in a recent conference a colleague had asked him about the XNA metabolism. The principal investigator then clarified that,

This particular researcher feels that one of the directions I should pursue is creating the machinery for the cell to make the XNA [nucleotides] *in vivo*. From building blocks that are easily accessible to the cell. So essentially create the XNA metabolism.

His colleague was interested in the XNA metabolism as an interesting research problem that could lead to high impact papers. But the principal investigator valued biocontainment and remained committed to acting responsibly by introducing safety features. He then continued,

And on multiple conversations, they just cannot get the fact that if I do that, then I'm weakening the containment, which is exactly what I'm building the technology for.

In this case containment is framed as both a design and an ethical issue, manageable through the properties that are embodied in microorganisms. He further explained that his colleagues probably did not understand that for him, “[the XNA metabolism] is an ethical issue. I cannot build a bridge that I don’t want to build, because that then undermines everything else I’m doing.” The principal investigator’s understanding of the commitment to not pursue XNA metabolism as an ethical choice is in line with a dominant framing of risk issues as ethical in molecular biology (Wright, 1994). What the principal investigator conceives as ethical principles bears relation with avoiding hazards or risks that new technologies may impose, and in this way, he sees it as a responsible practice. The principal investigator’s subsequent comments clarify this point:

If the premise is containment, if the premise is developing a technology that will tackle the risks that cannot be quantified, the risks are not pre-empt, sort of preempt risk, then any line of research that creates an exit route, undermines the containment.

He then explained that the chemistry behind his approach to xenobiology makes it very difficult for nature to overcome the containment. So, for the principal investigator, using “the resources that the funding bodies have given me for containment, to undermine containment... there’s an ethical issue there.” What is perceived as ethical depends on a political context. Decisionmakers, funders, and scientists share an imagination of the public according to which biocontainment is a worthwhile goal. This means that scientists pursue an agenda of biocontainment, following or giving signal that this is worth doing.

Biocontainment is a matter of controlling risk, as well as allowing control over access to the core of the technology (in this case, XNA-based organisms). This constitutes an ethical choice, and obeys an understanding of responsibility as accountability (Nissenbaum, 1996). If a scientist can ensure that a technology that he or she creates cannot be further modified, and perform as intended, is it a responsible conduct? As well intended as this attitude may be, this is problematic in the sense that it is not possible to ensure that technologies will be used in determined ways, or follow a script (Wynne, 1988). Users determine how technologies perform. It is very likely that if xenobiologists manage to produce XNA-based living organisms, these will be used and tweaked by users in ways that the original creators could not anticipate. Technologies of containment may be used for purposes that go beyond safety, as I have argued throughout this thesis. The relation between containment and control of access deserves monitoring. Containment technologies also embed beforehand relations of whom can modify the technology and have access to it. This entangles to questions over property rights, and commercialization of new technologies

Paying attention to matters of design brings the discussion close to ‘biosociality.’ Paul Rabinow (1992: 241-242) explains that “If sociobiology is culture constructed on the basis of a metaphor of nature, when in biosociality, nature will be modelled on culture understood

as practice. Nature will be known and remade through technique and will finally become artificial, just as culture becomes natural.” If the design of the XNA metabolism anticipates future modifications by other users and the responsible action of designers, to a certain extent it reflects the current organization of the life sciences, associated with the biotechnology industry and the production of value. Although xenobiologists seek to imitate nature by recreating existing genetic systems, in doing so, they extend particular relations and modes of operation of biological systems.

Decisions about technological paths are connected to multiple ramifications such as patenting, which has become an essential part of the knowledge production regime in place in which universities expect and favour the commercialization of research outcomes (cf. Berman, 2012). Control of new technologies involves control of intellectual property, an important currency for the commercialization of new technologies and career advancement. The assemblages that xenobiology enables can potentially concentrate ‘control’ in the hands of few researchers or owners, which raises concerns about the interests and goals of those in power. The scientists involved in biocontainment and xenobiology control the production and distribution of a synthetic amino-acid or XNA nucleotides. For instance, 16B commented that “everyone can synthesize DNA, and everyone can produce these compounds, not everyone, but is relatively easy to make this synthetic biology at home or with very basic equipment, as compared to other fields of science.” This applies to most of synthetic biology, which focuses on developing parts and engineering genetic circuits and metabolic pathways. However, 16B also comments that for xenobiology approaches, matters of control are different: “perhaps this interest in making bacteria or making some organisms to depend on synthetic chemicals is connected to the fact that if you now are the only source of that chemical, *then you have complete control on your production, right?*” (emphasis added). I aim to bring attention to the multiple motivations that are at play when designing and developing new technologies. The substitution of institutional and social mechanisms for governance in biocontainment could be used as built-in intellectual property protection (as explained in the previous chapter). If xenobiology is developed for exerting stronger intellectual property protection, how could this change the dynamics of the life sciences industry? Does this reflect a lack of support for existing governance structures which may be underestimated? This view coincides with Chan and colleagues (2015: 85), who wrote in their article on biocontainment: “In addition to its use as a biocontainment system, the Passcode circuit may find particular utility as *a tool for intellectual property protection*, where unauthorized growth of strains without the appropriate passcode molecules would induce cell death” (emphasis added).

Currently there are no commercial applications that employ xenobiology to gain a stronger protection of intellectual property rights or fence off industrial espionage as some scientists suggest. However, successful approaches in xenobiology or related biocontainment technologies do have the potential to become an ‘obligatory passage point’ (Latour, 1987), providing privileged access to a few scientists well positioned in the field. Patents in the life sciences have been criticized for limiting the access for research tools to conduct fundamental research (Nottenburg et al., 2002; Walsh & Hong, 2003). At stake in xenobiology is the control of basic building blocks, like XNA nucleotides, synthetic amino-acids, or modified microbial strains, without which further research and development of xenobiological organisms would not be possible. The xenobiologists I spoke to were not interested in creating a research niche that only they could occupy; in other words, monopolizing a discipline. Interviewee 5C explained that he would like to see many more researchers in the field and there was plenty of room for more researchers and different approaches in xenobiology. In **Chapter four** I argued that much of the visions of xenobiology were deployed to attract resources and attention to the field. When I asked why the community of xenobiology was small, the response was that it is very costly to conduct research in the field, vast resources are required to produce a worthwhile discovery. Because xenobiology is based on tacit knowledge and requires access to materials or reagents that are not commercially available.

I asked the principal investigator about patenting some of the research in xenobiology conducted in his laboratory. He explained that this depended on an agreement between participants in different consortia. In principle, the technologies that are developed could be licensed, but licensees would “not develop *a way of metabolizing* those [XNA] nucleotides. [Licensees would] accept that you will not develop a way of manufacturing those nucleotides *in vivo*, because *that would break the containment*” (emphasis added). The principal investigator was conscious about unknown outcomes that were beyond his control, according to his concern that the ‘containment’ that xenobiologists work hard to build could be dismantled if an XNA metabolism were developed. This reflects confidence and a belief in design as the locus of governance of technology. At the centre of these competing visions of what purpose an XNA metabolism could fulfil, one of responsibility and safety through design, or one of advancing the frontier of knowledge, is the social role that research in the life sciences should play. When it comes to developing (or not) an XNA metabolism, what is at stake is the level of responsibility attributed to the users of the technology. By limiting the possibility of developing an XNA metabolism, users are deprived of moral choices, and the developers of the technology avoid future liabilities by misuse. Scientists maintain a privilege to determine what counts as safety and as responsibility.

### 6.3.3 Lessons from ‘Genetic Use Restriction Technologies’ for xenobiology

The analysis of biocontainment as a form of responsibility in biotechnology should consider the motivations of researchers and underlying power structures. The tension between biocontainment, responsibility and control—both in the form of controlling the outputs of the technology and controlling its access—is not unique to xenobiology. Following the discussion about responsibility as design, and the potential monopoly of researchers over the production of XNA-related reagents, it is useful to extend this analysis to similar technologies in the life sciences with the power to dominate the cycle of life, such as ‘Genetic Use Restriction Technologies’ (GURTs), developed by Delta & Pine Land (D&PL) and the U.S. Department of Agriculture (USDA). Both GURTs and biocontainment restrict growth and determine death. The Canadian NGO RAFI (now ETC Group) in 1998 coined the term ‘terminator technologies’ for GURTs (cf. ETC Group, 2007). This genetic engineering technology used in crops can render agricultural seeds infertile after the first generation, thus creating a need for farmers to return to the seed-producer to re-purchase seed each season. ‘Terminator seeds’ have been the subject of controversy mainly for their consequences on the welfare of farmers (cf. Kluger, 1999; Service, 1998). Although agricultural crops are different from engineered microorganisms, they have in common with xenobiology that their growth and propagation depend on the supply of a manufactured chemical. Both have at stake the control of life.

Thom van Dooren (2007) observes the potential of ‘terminator seeds’ to disrupt human-plant relationships. He argues that seeds incorporate built-in practices, associations, and relationships of kinship—ways of life—are at stake in the ‘choice’ of a seed.<sup>165</sup> His analysis points out implications of terminator seeds, such as the impossibility of improving local plant varieties (which inhibit the co-evolution of crops with social environments), challenges for food security, and the mishandling of seeds (cultivating seeds that are sterile). Van Dooren also argues that the technology is tightly coupled with the enforcement and policing of proprietary ‘rights’ of seeds. In his view, terminator seeds are designed to circumvent existing intellectual property frameworks. First, the protection of property rights could theoretically work in perpetuity, unlike a patent which expires after twenty years. This would create a negative incentive to challenge the validity of a patent, since it works outside the system that could host such disputes. This serves to avoid the difficulties and cost of enforcing patents, not only in surveillance and litigation, but in countries where patent protection is not properly applied (for example in Argentina, with the case of soybeans). The second point

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<sup>165</sup> See Jasanoff (2005b) for an analysis of genetic engineering of crops and their relationship with local contexts.

about the political economy of terminator seeds that Van Dooren proposes is a concern about corporations having control of production. For seed production, farmers would become dependent on “trade and economic systems that are vulnerable to a variety of different disturbances, such as war, civil disorder, and natural disasters” (ibid., p. 82).

What lessons can be derived for xenobiology? Although GURT crops were not commercialized, parallels can be drawn as both technologies invoke governance by design. I did not get the impression that ‘xenobiologists’ want to develop technologies that circumvent difficult and controversial issues around patents in the life sciences. Rather than accusing xenobiology of embedding intellectual property features, I flag such concern to open up and be clear about the purposes and motivations of these technologies (cf. Stilgoe et al., 2013). Establishing parallels between xenobiology and GURTs is not fully accurate, as they present different features and modes of action; the applications of xenobiology are not necessarily relevant for food safety, or farming communities, and it is not clear who would be affected by a regime in which control is embedded in the microorganisms themselves. It is not yet clear who would use future xenobiology-based technologies, this is a blank canvas. This poses a challenge of imagination, of thinking how GEMs will be used in a market that needs to be created, for uses that are still to be defined.

Xenobiology and GURTs share a predisposition of controlling life’s essential properties of life and death, both reflecting how the biological is also social and enables new forms of property, writing ownership into genetic systems. Such control and tendency to disrupt existing networks, trade practices, and notions of the living, is prone to cause public discomfort. As Sunder Rajan (2006) has noted, emerging biotechnologies are coproduced with the market logics within which they emerge. Hence, the artefacts of xenobiology will be restrained by specific forces of biocapital that restrict its circulation and values in specific ways. Biocontained organisms are part of a knowledge production regime that favours control and reductionism and are prone to incorporating mechanisms for reinforcing such dynamics.

## 6.4 Summary and conclusions

In this chapter I argue that biocontainment in xenobiology is mobilized as a form of responsibility that relies on how the public is imagined. Such imagination determines efforts to develop technologies that are adopted and received by society. Public acceptance imposes a *limit* that xenobiologists aim to renegotiate (in addition to the boundaries of life). Containing microorganisms is also about controlling public opinion and establishing the rules of emergence of new technologies, following the sociotechnical imaginary of

controllable emergence that I propose. Nevertheless, I make the case that public debate cannot be controlled through biocontainment, in part because it does not fully address the reasons why publics may resist new technologies. Biocontainment works for scientists as they imagine the public as fearful of new technologies. Such debates fail to engage complete picture of the causes of the genetically modified food controversy in the 1990s, and other reasons why science as an institution has lost credibility in the public, including other controversies not related to genetic engineering. Such debates incorporate the purposes of innovation, the uses of new technologies, and the economic and political structures that sustain the current knowledge production regime, more and more inclined toward achieving 'impact' and commercializing research for boosting the bioeconomy.

That scientists draw on explanations of their own making to account for the perceived imagination of the public as being resistant to emerging technologies makes a confusing picture, since I show in this chapter that the public, as heterogeneous as it may be, shares a preoccupation about the safety of new technologies, and the risk of genetically modified organisms spreading out of control. Hence the importance of providing an overview of the constructed character of biocontainment, since scientists do not agree that genetically modified microorganisms are a hazard for the environment, but nonetheless recognize that this is a matter of public policy that extends beyond the realm of scientific questions to involve questions about risk and the public good. Lack of proper handling of public debates about genetic engineering, or the lack of opportunities for deliberation, serves to reinforce the framing established since the 1970s that the matter of concern that deserves being taken seriously is safety, rather than values, and considerations about life and the natural world.

Because the safety of genetically modified microorganisms cannot be established with certainty, cannot be known, I claim that biocontainment serves as a *technology of compliance*. Developing built-in safety features serves to meet the *perceived* requirements of a society that is not fully on board about technological progress, but these requirements are neither scientific nor regulatory. They serve to match an expected feature of technoscience—that biotechnology be safe. Embedding institutional and governance features in the design of organisms it serves to enable other aspects like intellectual property rights and the control over access and distribution of xeno-organisms or their derivatives, besides the release of genetically modified microorganisms into the environment. A consequence of technologies of compliance is that they can potentially inhibit public discussions about the purposes and ends of innovation: If scientists manage to appease what they perceive as the needs of the public, this restricts the need to genuinely engage with the public and address the social challenges that biotechnology could fulfil. The very possibility of commodifying and

standardizing safety via biocontainment, as a one size fits all approach, should also be the subject of scrutiny.

A second consideration that I bring to the fore is that biocontainment is a form of responsibility. The understanding of responsibility of scientists is consequentialist in the sense of *controlling* the outcomes of xenobiology. Nevertheless, there is a tension between scientists taking responsibility and taking control; ensuring control over engineered microorganisms does not imply that responsibility is being followed. Nevertheless, the discussion opens the door to think about responsibility in science from the perspective of scientists. Overall, as questions of xenobiology and responsibility centre around the degree of control that can be exerted over organisms, and safety is associated with such control, my analysis aims to highlight the importance of considering that debates over safety in genetic engineering are entangled with questions about naturalness, that publics highly value.

With this chapter (and the previous one) I finalize the analysis of a sociotechnical imaginary of controllable emergence, according to which design principles and control at the level of the organism can work as governance mechanisms to appease a public constructed as fearful of new technologies. In the next section I develop further on themes of control and uncertainty, and reductionist versus systemic thinking in xenobiology, with a focus on the barriers that limit scientists to consider the wider ramifications of their research.



## 7. Embracing uncertainty in the real world

### 7.1 Introduction

Biocontainment emphasizes a particular aspect of risk that turns safety and values into a managerial approach, not taking into consideration all possible scenarios. In xenobiology, biocontainment is the embodiment of an imaginary of governance in which risks are manageable and benefits are unbounded. Previous chapters in this thesis have addressed how scientists imagine (or think) about life and the public, arguing that governance by containment ignores ramifications, assumptions and values that do not fit into a narrow framing of risk. Research in xenobiology incorporates socio-political themes that are also biopolitical and environmental, reflecting a particular understanding of how the world (life itself) is arranged, in terms of units and not in a holistic way that treats biology as ecosystems, as biomes (Helmreich, 2011). In this chapter I address the way scientists think about risk and safety, and what limits holistic approaches that acknowledge uncertainty and the complex interactions that organisms display with their environment or habitats. The tension between controlling uncertainty and achieving certainty—in controlling life and earning public trust—lies at the heart of xenobiology. The contrast between control and uncertainty is the foundation of the social contract for science. For instance, Callon, Lascoumes, and Barthe (2009: 119) write,

Shut away in their laboratories, researchers are accorded complete autonomy, with increasing budgets, but in return, and this is the object of the delegation, they must come back with confirmed facts, as solid as the hardest granite. Autonomy and billions of euros is the price the collective pays these luxury mercenaries whose sole mission is to produce knowledge purged of all uncertainty.

To which they add,

Do what you like in your laboratories, spend as much as you need, but do not come back to see us until you are sure of what you put forward, before you can describe with the greatest certainty all the possible worlds in which we could live!

Even though STS analysts have criticized reductionism in the life sciences (cf. Wynne, 2005), little attention has been given to what alternatives would look like, such as an expanded framework of thinking that gives priority to ecosystems instead of organisms. In the life sciences, Coole and Frost (2010: 15) write, “Material phenomena are increasingly being conceptualized not as discrete entities or closed systems but rather as open, complex systems with porous boundaries.” Moreover, Joan Fujimura (2011: 75) speaks of leaving aside notions of dominance over nature or metaphors from cybernetics, to think about symbiosis as the “coexistence of organisms of different species in interdependent relationships where each benefits the other.” In this chapter I suggest reasons that inhibit

progress in ways of thinking that deal with the complexity of the biological world. Xenobiology cannot escape this question since one of the premises of biocontainment is providing control of genetically engineered microorganisms, enabling their release in open environments. Responsible release should not be about ensuring control before release takes place but having in place proper methods to analyse risks and benefits and allow the participation of stakeholders in decision making.

Research in synthetic biology has given less attention to the relation of synthetic organisms and their environment, focusing on reducing complexity at the level of the cell. Even systems biology, which embraces complexity, seeks to understand mechanisms at the level of a cell, but not its surroundings (Kogge & Richter, 2013). Attempts have been made to explore the opportunities or challenges that synthetic biology presents for conservation (Redford, Adams, & Mace, 2013) and introducing questions about ecology and the environment, that require overcoming interdisciplinary barriers between synthetic biologists, engineers, and natural scientists (Kuiken et al., 2014). In this thesis I aim to contribute to the STS literature on synthetic biology (and xenobiology) by drawing lessons from collective and real-world experimentation. In previous chapters I have explored the imaginaries that drive the emergence of xenobiology with respect to shifting attitudes toward life (**Chapter five**), governance by design (**Chapter five**), and an understanding of responsibility as control and compliance to public expectations (**Chapter six**). In this chapter I take a detour from the previous chapters to interrogate how scientists think about risk, and question difficulties for thinking about xenobiology in holistic terms, for instance considering the ramifications of xeno-organisms for the environment. I suggest that thinking about ‘experimentation’ should also take into account thinking about platforms for deliberation, as well as contrasting worldviews and values embedded in the technological trajectories that xenobiologists may follow.

The outline of this chapter is as follows. I first consider in **section 7.2** reasons for which research in xenobiology tends to focus on the molecular level, often ignoring considerations of ecology and impact on the environment. I argue that research in xenobiology is conducted in laboratories where the goal is to reduce complexity to allow the creation of novel proteins and molecular assemblies, goals which do not benefit from thinking at a larger scale about the relation of experiments with their environments. In short, I claim that the scientific practice of xenobiology is prone to ignoring questions of complexity and ecology. In order to broaden these concerns, in **section 8.3.1** I address whether concerns about ‘toxicity’ can

serve to raise awareness about the environment.<sup>166</sup> For researchers in xenobiology the main concern about toxicity is that XNAs are not harmful for human health.

Subsequently, in **section 8.3.1** I consider institutional factors that shape how scientists think about risk, among which I analyse lack of resources and expertise for evaluating risks, as well as a lack of recognition by peers for such type of experiments. Last, in **section 8.3.4** I provide an overview of novel approaches to the release of genetically modified organisms with gene drive technology, drawing lessons for experimentation in xenobiology. I argue that questions of experimentation are tied to questions of governance and platforms for deliberation.

## 7.2 Reductionism in xenobiology

I have argued that xenobiology aims to redefine what we understand as life in terms of being defined by its genetic system. As xenobiologists challenge the limits of what is biologically possible, their locus of intervention is the genetic machinery of the cell. This reflects a degree of reductionism, understood as the approach to analyse a larger system by breaking it down into pieces and determining the connections between the parts. This assumes that the isolated molecules and their structure have sufficient explanatory power to provide an understanding of the whole system. Reductionism has been successful for experimentation in the life sciences, dominating thinking in biology for the last half century (Van Regenmortel, 2004). This is in line with my fieldwork in the laboratory where I observed that the focus of the experiments has been to create novel tools (i.e., enzymes) to manipulate XNA material, or integrate tools into cells. As xenobiologists employ methods from molecular biology and protein engineering to develop novel molecular machinery that can replicate and propagate information in XNA material, their focus of intervention is enzymes and assays. They need to construct in the laboratory novel proteins that can work with XNA, based on modifying existing enzymes that work with DNA. This is conducted in the bench, with assays that disassemble the complexity of cellular interactions and allow the researcher to check for particular functions of a desired protein, (i.e. whether an enzyme can create XNA segments or sequences) (See the discussion on molecularization in **Chapter Four**). If the goal is to develop a functional XNA molecular machinery, it is not a criterion for success how future xeno-organisms will interact with their environment. Research efforts for developing an XNA machinery take place in the laboratory under controlled conditions that leave very little

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<sup>166</sup> Toxicity can be understood as (potential) harmful effects of chemicals and biological systems associated with xenobiology, for instance the accumulation of XNAs in the environment that may be turned into chemicals that are carcinogenic or teratogenic.

to chance. For example, interviewee 11A highlights the laboratory is an essential place to address questions about biology,

[Synthetic biology] is more trying to understand a phenomena that's maybe has been observed in nature, and you know want to try to understand what it takes *to recreate that in the lab*. And then you can maybe have the opportunity to go beyond that push the limits. Is this the way it is in nature because it has to be like that? (emphasis added).

Xenobiologists are concerned with understanding life from a reductionist perspective. Life is understood as unitary, as the equipment that enables an organism to perform functions and reproduce. From a systems perspective, organisms are understood as part of a web, of a habitat or ecosystem in which attention is given to the interactions between multiple organisms, not the genetic makeup of particular organisms. In ecosystems long-term sustainability is dictated by feedback loops that redistribute energy and resources through all participating organisms. The experiments I observed in the laboratory involved molecular biology, a field characterized by a tendency for researchers to work in individual projects, with each researcher having a dedicated personal space (the bench) in which experiments are prepared and continued in instruments that are shared with the laboratory or with other laboratories. During my fieldwork I had the opportunity to observe experiments of two different types of projects, one related with the production of novel peptides with tools of molecular biology, and the second, aligned with the goals of xenobiology, of developing an enzyme that would be part of an XNA 'molecular machinery'.<sup>167</sup> I also helped the former experimenter with 'mundane' tasks of gene cloning, that nowadays have become routine operations in molecular biology.<sup>168</sup>

The distinction between the modes of experimentation and scientific practices in xenobiology and molecular biology brought my attention to the *source* of tools used in practices and experiments. Manipulation of cells and biological molecules (and macromolecules, like DNA or proteins) at the molecular level is enabled by chemicals (like dyes and reagents like chloroform) and materials adapted from natural sources; source materials are pre-constructed, so nature is rarely found in the laboratory (Knorr-Cetina, 1983). The most important example is restriction enzymes, discovered in the 1970s, which enabled the emergence of genetic engineering. The technique PCR, for instance, arguably the most widely used technique in molecular biology worldwide, relied on a heat-stable polymerase (commonly known as TAQ polymerase) derived originally from *Thermus aquaticus*, a bacterium that lives in hot springs and hydrothermal vents.<sup>169</sup> Taq polymerase,

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<sup>167</sup> I have changed the term that scientists used in order to protect their anonymity.

<sup>168</sup> For example, interviewee 14A remarked, when asked how he would classify the type of work he does in the lab: "what I do is mostly molecular biology. The day to day work that I do is just mostly bench work, just going in and doing PCR, and sort of very routine things like that."

<sup>169</sup> For the discovery and characterization of DNA polymerase I (Family A) from *Thermus aquaticus* (Taq), see Chien et al., 1976.

restriction enzymes, CRISPR–Cas9 and other molecular tools originated in processes that occur naturally in living organisms. This is important because what scientists can accomplish in the laboratory is dependent on what has been accomplished in *nature*. In the laboratory I studied I conducted a gene cloning task to assist a doctoral student’s project. The experiment involved using PCR to fabricate a plasmid which would contain a gene of interest, which would be propagated many times once inserted in a bacterium. Since we had introduced a series of mutations in a specific plasmid, the experimenter I was working with needed to get rid of the ‘old’ plasmid, so that only the new, ‘mutated’ plasmid would remain. For this, there was a restriction enzyme that could distinguish between bacterial DNA (which would be methylated) and artificial DNA (synthesized via PCR) and would cut the bacterial DNA. I expressed my surprise to the laboratory member when he explained to me that distinguishing among bacterially produced and PCR-produced DNA was possible. The laboratory member replied that “all of molecular biology is finding happy coincidences.”

A more ‘holistic’ approach to redesigning life would consider living organisms as part of ecosystems, considering their capacity to perturb ecosystems in unanticipated ways. Genetically modified organisms are brought into the world devoid from an evolutionary history. They come from nowhere, and do not have a shared past with other living beings (Bensaude Vincent, 2013c). A common past also involves having been subject to similar evolutionary pressures and adjusting to other organisms in an ecosystem. Questions around ecology or ‘holism’ have a hard time entering the laboratory, where the reasoning behind conducting experiments is reductionist, constraining the types of questions asked and the ways of thinking. However, such questions are present in other settings and disciplines. A case I point was a panel discussion titled ‘Xenobiology priorities’ in a workshop on ‘xenobiology, biosafety, and biosecurity.’<sup>170</sup> The panel included synthetic biologists and xenobiologists, including Philippe Marlière, and scholars in STS and Political Science. The STS commentator commented:

Why is there so much reductionism in biotechnology? Reductionism is only one way of interrogating our existence. There’s holism as well. *There are holistic fields, like ecology*. The funding for reductionist biotech is massive. It doesn’t mean it’s bad. Massively greater (emphasis added).

This comment came after the researcher questioned the focus of members of the panel, who took for granted that xenobiology should move forward. This came to the surface in the organization of the laboratory and its focus on developing tools and assays to manipulate cells to depend on XNA does not benefit from asking questions about ecology or systems thinking. On a different note, Philippe Marlière has also conveyed that xenobiology and ecology do not go hand to hand. In an interview by Anna Musso about the study of Floyd

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<sup>170</sup> See footnote 59.

Romesberg laboratory in 2014 for the French newspaper *L'Humanité*,<sup>171</sup> when he was asked why to dedicate a career to the creation of artificial living organisms? Marlière replied,

The possibility of creating new forms of life has always raised as many fears as passions” ... “It is perfectly legitimate that a breakthrough technology raises questions in the general public about risks to health and the environment. This is why it is important to explain the methods and the positive ends of these inventions.

Then, Marlière brings ecology into the discussion:

The difficulty with many ecologists is that in the debate, reason never takes over. Environmentalism [L'écologisme] is unfortunately sprinkled with irrational doctrines, one might think religious, in fact frankly superstitious.

Marlière continues, associating environmental thinking with rejection of xenobiology:

To assert that if one reshapes life, it necessarily carries misfortune, whatever the modalities or the reasons for doing it, it is superstition. However, issues such as genetic pollution, which are suspected in the case of GMOs, can and must be approached with no passion, exercising its reason to develop reliable and publicly justified countermeasures.

Marlière's comments suggest that ecological thinking is irrational, not adherent to scientific reasoning. For him, addressing such concerns like 'genetic pollution' is possible in the laboratory as long as organisms are equipped with commands and tools to behave in a certain way in an environment, what Ben Hurlbut calls a 'travelling jurisdiction' (Hurlbut, 2017b). In the workshop about xenobiology and biosafety mentioned above,<sup>172</sup> in the same panel Philippe Marlière pointed out the difficulties (in terms of missing theoretical tools) to think about xenobiology in a wider context, asking:

What it is to change an ecosystem. This question, what is the real impact, or the potential impact, or whatever, and I think, and I state, and I've said many times, that there is absolutely no available formal system for talking seriously about that. Not at all. Nobody can say or have any model, of what it means to invade an ecosystem; and it is not the fault of synthetic biologists, it is the fault of ecologists.

Marlière downplays the disciplinary rigour of ecology, reflecting the distance that divides the two disciplines, in which xenobiology (or synthetic biology) is portrayed as more scientific than ecology. If pioneers of xenobiology consider that large-scale thinking as occurs with ecology is not necessary nor relevant, it is difficult to incorporate such questions in the ethos of xenobiology. Precisely, biocontainment aims to place the locus of control on the organism, fitting it with properties to unfold properly independent of an environment. Organisms should not be conceptualized as being independent of an environment if they are ever to be released in open environments. The discussion about the role of ecological or systems thinking in xenobiology goes beyond a disciplinary dispute. This is due partly to xenobiology being about what can be controlled or accounted for in the laboratory, ignoring what cannot be controlled. Incorporating systems thinking is a challenging task, because

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<sup>171</sup> See footnote 10.

<sup>172</sup> See footnote 59.

there are no clear parameters on how to think about safety-by-design as a question of ensuring a particular behaviour of a microorganism in an environment where so many variables are uncertain.

In rethinking life and challenging the limits of what is biologically possible, scientists are also reconfiguring long held views of what is valuable in nature, and how we (as humans) relate to nature. With its potential to question what we understand as life and its origins, xenobiology opens two avenues for reflection. On the one side, there is the question that life is flexible, malleable, and can be manipulated in ways that scientists are defying. In principle, work in biology is limited by the tools that scientists develop, imitating existing tools in nature (like the DNA replication machinery) and limited by their imagination to conceive what is desirable and what are good scientific questions. On the other hand, given the difficulties that scientists face in advancing the field of xenobiology, and their need to employ methods from (directed) evolution, makes it worth asking how unlikely it is that life came into being, and how in that case it is intrinsically full of value.

Questions about the value of life have passed to a second plane. In previous chapters I addressed whether synthetic organisms will present unanticipated risks is not knowable based on current evidence. However, it is worth considering scenarios in which things deviate from expectations, as Victor de Lorenzo (2010: 930) writes,

Unlike the earlier cases where it is possible to find precedents to the risk questions and to foresee possible answers, the uncertainties raised by artificial/orthogonal life *constitute a completely unknown territory*. It is intuitive that such systems should be the safest, because they could not interact or interfere with the extant biological world; however, one can also conceive of plausible threats (emphasis added).

The framing of safety as unknowable resonates with a view that was widely exposed in my conversations with scientists, for whom there is no downside of embedding safety features in engineered microorganisms. For some, safety might not be a priority, but it is good to have safety features on board; it would be stubborn for a scientist to be against safety. The underlying issue, as this chapter aims to develop further, is how is safety–risk are framed, and who gets to participate in such framing. Whereas De Lorenzo draws attention to the uncertainty that presents ‘artificial’ or ‘orthogonal life,’ the response to these concerns, embedding safety features, displays a willing to control such uncertainty—an illusion of control.

In this section I have made the case that thinking about the impact on ecosystems is not a priority in xenobiology. This is owed to the conditions of knowledge production in the laboratory, where the goal is to reduce life to its minimal components and mimic them. Bridging the gap between disciplines like xenobiology and ecology may prove difficult because each field has its own epistemic assumptions, terminology, and paradigms. Hence

creating a ‘trading zone’ (Galison, 1997) would be necessary, but this in turn requires a need for xenobiologists to think outside the laboratory bench to consider the complexities of ecosystem dynamics. This would be possible if the promise of releasing microorganisms to the environment is taken seriously and acquired a more active role in the agenda of xenobiology. Not including questions about the environment in the expanding definition of life that xenobiologists propose, limits possibilities for social learning (Stilgoe, 2018), which is crucial given that experimentation in xenobiology (at least in open fields) involves all of society. In the next section I explain how concern about potential ‘toxicity’ of XNAs for the environment is a way of considering the relation between XNA-based microorganisms and their environment.

## 7.3 Considerations of xenobiology and release of microorganisms

### 7.3.1 Experimentation as testing toxicity

Synthetic biologists and xenobiologists have worked towards a vision of biocontainment as a strategy to enable the release of microorganisms in open environments. Nevertheless, hype about release must be weighed against potential unintended consequences for the environment (Moe-Behrens et al., 2013). Through my engagement with scientists I intended to raise awareness that the impact of xenobiological organisms was a matter that went beyond escape highlighting the uncertainties of release. I wanted to stress the possibility that full control of synthetic organisms may not be achievable, prompting reflection on how this would impact design and governance practices. Some authors have called for considering environment impacts; for instance, Dana and colleagues (2012: 29) consider that ‘synthetic microbes’ are a different category from previous efforts in engineering life, and their implications are different as well:

No one yet understands the risks that synthetic organisms pose to the environment, what kinds of information are needed to support rigorous assessments, or who should collect such data. These questions have been raised before, with genetically modified seeds, for example. But unlike transgenic crops, synthetic microbes will be altered in more sophisticated and fundamental ways (such as elimination of metabolic pathways), making them potentially more difficult to regulate, manage and monitor. They might also have environmental impacts that are difficult to predict.

And proponents of xenobiology have expressed concern about the potential of xenobiology-related chemicals to harm the environment. The discussion tends to centre around issues of toxicity as a negative environmental impact. For example, Schmidt & de Lorenzo (2016: 94) write that,

Xenobiology approaches look more promising for building genetic firewalls that will allow an extremely high level of containment in heavily engineered and synthetic organisms. Yet, *introducing synthetic chemicals in biological agents creates its own problems if xeno-GE organisms are released into the environment*. The effects of non-standard biomolecules, for example, synthetic



amino acids, XNA, alternative base pairs, among others, in living systems is largely unknown, let alone their potential toxicity and allergenicity (emphasis added).

This passage sets a distinction between biological containment, and less explored aspects like the toxicity and allergenicity of chemicals used in xenobiology; it makes implicit the uncertainty that xenobiology-based interventions trigger. Thinking about uncertainty is difficult because it involves lengthy time-scales and effects that are not always visible or measurable. For example, interviewee 8B, after explaining that they are confident in the ability of bacteria and ecosystems to adapt to pressures presented by new chemicals and new types of microorganisms, commented that “there are general safety issues in terms of the chemicals we use and that kind of thing. [...] In terms of the specific dangers of our systems, in the far future, if things go really well, in terms of the technological development, that could be a concern, but at this point it’s not really.” On the contrary, interviewee 2A expressed concern for the difficulties of identifying XNA reagents. Risks depend on the instruments and mechanisms in place to detect them. For 2A,

In my particular field [i.e. xenobiology] we have the opportunity to create new molecules which don’t exist in nature. And one of the things that I worry about is that we will create molecules which are very toxic, and I’m thinking particularly of the potential exposure of researchers to that. [...] If I create a new molecule, and it’s super toxic, it’s going to be difficult to find out until you really find out.

The toxicological impact of XNA-related materials was one of the topics I discussed with the laboratory group. I did not focus on defining the term properly, my goal was to use toxicity as a topic that would spark valuable conversations about responsibility in science. Toxicity is one of the main concerns about safety in nanotechnology (Kelty, 2009; McCarthy & Kelty, 2010). Contamination of water, air, and land caused by industrialization and urbanization are among the key feature of our modern era, all having in common the release to the environment of chemicals that are either not found in nature or that affect the chemical balance of ecosystems. In an interview, the principal investigator explained that XNA nucleic acids are usually derived from candidates intended to be used as pharmaceuticals in humans, so they have been selected for not being toxic: “That’s one of the reasons how to select XNAs, to be careful that they are non-toxic, and they are tested in living systems to see. If they are toxic for a living organism, even *E. coli*, you cannot use it as XNA, because the bacteria will die out and your experiment is gone. So, it should be, and it’s selected as based on [being] non-toxic.” This understanding of toxicity as the potential harm to living cells was predominant with the scientists I talked to. It keeps the impact of the chemicals at the level of the organism, or the organisms surrounding it. The principal investigator of the laboratory further explained that the XNAs that the laboratory uses have been proven to be safe for the human body, as they have been subject to previous tests as potential anti-cancer drugs. But he recognized that there might be unforeseen side effects, for example in terms of how the compounds are metabolized in the liver, or they may interact with receptors in the body.

This approach to toxicity is manageable in the laboratory, again influencing how problems surrounding xenobiology are framed. In the same interview as above, the principal investigator expressed “that is not to say that [XNA and associated materials] cannot be toxic. It may be toxic. In which case, the idea ... to push forward to *in vivo* evolution, so you identify or simply fix what’s causing the toxicity.” The principal investigator recognized the need to address safety since as he expressed, “there is a track record in the field [the biotech industry] of things that are not safe.” This also applied when products of xenobiology would reach the market. In his view, if scientists do not address the issue, the market would take care of it, as safety is important for everyone involved. As toxicity can be subject to interpretation and framing, it is possible that is used as an excuse to not engage with environmental aspects. Scientists may claim that they are being responsible by addressing concerns of toxicity for humans, which could exclude them questions about the environment.

Experiments in the laboratory determine what is knowable and achievable, through the mediation that instruments guide between the experimenter and recreated phenomena. It is possible to measure whether cells are affected by exposure to certain chemicals, but how the same chemicals might affect an ecosystem, or be degraded over time, requires a different set of expertise and timescales. Research does not reduce uncertainty but increases it (Gross, 2010a), and experiments cannot tell what they do not measure, leaving a gap in the knowledge produced. Scientists could argue that if XNA materials were not toxic to cells, they should not pose a problem for the environment. They also place confidence in modelling and its capability of reconstructing reality, in a pixelated picture; modelling is inherently biased by the parameters, previous knowledge, and assumptions that research include in their models. Still, modelling provides an illusion of reality that allows making decisions and moving forward with plans for experimentation. Interviewee 16A suggested, for example, that there were experimental setups with different scales that could provide useful data to assess ecological impact, like the use of *ecospheres* or *ecotrons*, which function like ecosystems at a small scale. Interviewee 29A also remarked the role of modelling for addressing the ecological impact of genetically modified mosquitoes, commenting that “in principle [models] represent a pretty good model of what will happen in the field,” noting that this depends on the scale being used. Nevertheless, gathering more data (and experimental platforms available) is different from the type of answers that are pursued. My point is to highlight the need to keep an open perspective about the downsides of certain outcomes of xenobiology, without focusing exclusively at the individual level, like matters of horizontal gene transfer. This type of thinking is exemplified by Wright and colleagues (2013: 1231), who write:

Further thought is required on how to design synthetic constructs and microbes to be intentionally out-competed over time. For this research to progress, *more quantitative data are*

*needed for how GMMs perform in sample environments.* The current lack of in-depth testing means that it is hard to accurately assess which safety mechanisms and designs are best at preventing ecological invasion and HGT [horizontal gene transfer] (emphasis added).

Thinking of the environmental impact of xenobiology chemicals has much to do with the instrumentation and tacit knowledge available in a xenobiology laboratory, which enables advances toward *in vivo* xenobiology. This was evident in discussions with the members of the laboratory, which were also enriched by using ‘toxicity’ as a proxy to consider the potential downsides of xenobiology, and uncertainties that could arise from research in the field and its eventual deployment in the real world. The narratives that scientists employ to conduct research determine the actions they will take to evaluate risk. If toxicity is understood as the harm that XNA reagents can cause to cells, it excludes from the conversation questions about ecological impact. Such narratives and shared understandings are part of institutional structures that support the advancement of a field of xenobiology, as I show in the upcoming section. Reductionism in the laboratory involves the types of questions that are asked, and also what researchers are expected to evaluate and investigate. If questions about undesired impacts of technologies are not brought to the laboratory, and reinforced through regulation, grant application requirements, or publication standards, it is difficult for new fields to advance in responsible ways. With these questions in mind I facilitated groups discussions as I explain in the following section.

### 7.3.2 Barriers for evaluating risk

Drawing from **Chapter four**, ‘navigation’ in xenobiology can be seen as touring uncharted territory: what will be found cannot be determined in advance. If researchers walk into the fog, it is questionable what accountability can derive from the decisions they make a future that is not visible in the mist. In my fieldwork, the principal investigator of the lab highlighted three limitations for thinking about responsibility, emphasizing that researchers *do care*; first, that researchers in the group had not been responsible for obtaining their own funding, which would have given them the opportunity to engage with that wider ramifications of their research, they entered already planned projects. Second, given the pressures for obtaining results and limited resources, choices have to be made in the laboratory; where deep thinking does not particularly help to ease such pressures. Third corresponds to timescales, as researchers are unlikely to remain in a single position to see significant developments of their project. The expectation is that each researcher provides incremental change which achieves a significant development over the course of a longer career, which may comprise different developments in different laboratories. In what follows, I address these considerations with a focus on how researchers think about biocontainment and risk in the laboratory and the scientific community.

I used the uncertainties associated with the development of xenobiology and its style of experimentation as a platform for discussing ideas in the laboratory that would not normally appear otherwise in conversations. In the last group discussion, I addressed possible outcomes of xenobiology, including environmental impact (toxicity). During the discussion, I showed a slide with quote from Markus Schmidt (2010: 328) that refers to the XNA metabolism (see previous chapter), in which he proposes ten “safety improvements [that] the following biological and technical specifications would have to [meet].” I highlight two aspects:

(iii) Natural organisms must also not be able to produce these essential biochemicals, to avoid a symbiotic relationship with XNA.” [the XNA metabolism];

And,

(ix) XNA must not be a recalcitrant chemical, but should act as food for natural organisms after its death/destruction”, the latter related to the environmental impact of XNA as chemicals.

These design principles that guide the agenda of xenobiology and command decisions taken in research projects, provided a good basis for meaningful discussions about the ramifications of xenobiology and systemic considerations.<sup>173</sup> When I talked about the ten ‘safety improvements’ that Schmidt proposes, the group commented on the difficulty in carrying out tests with XNA reagents due to the scarcity of such reagents. Synthesising XNA-related materials is difficult (it is also very costly) because it requires advanced chemistry skills to produce XNA even in small quantities. A researcher commented, reflecting epistemological limitations with the testing of XNA-related materials, that “you can test some things, but then, how safe is that? Where is the point where you say, OK, this is safe enough? I’m happy enough with the results? Where do you get the 95%?” This ambiguous territory, in which certainty cannot be established, where ‘what is safe enough’ cannot be determined by experimentation, lends support to what is at stake involves different actors of society, and willingness to accept and negotiate risks, as long as the benefits and negative consequences (at least what is known) are discussed. But the opposite also applies. For scientists, it seems that if such certainty cannot be achieved, decisions about it are outside their agency. Afterwards the discussion shifted to the application of drug or food safety evaluation models to synthetic biology. Participants commented that the limiting factor consists of having sufficient amounts of material to test. In this regard, a member of the laboratory remarked that organisms are different from chemicals because ‘biology can multiply.’

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<sup>173</sup> Some researchers in the lab were not familiar with Markus Schmidt, which reflects that his agenda has not been completely acknowledged by researchers in the lab.

One last remark deserves attention –the principal investigator of the laboratory proposed to establish what he called ‘trigger points’, which I understood as a form of *stage-gate*. In his words,

We have a limited amount of thinking that can be done at this stage [of research in xenobiology]. So, some of these things, they have to be *trigger points*. So, until you have an organism, there’s little value in thinking kind of what’s the evolutionary fitness of the new organisms... Because there’s nothing you can do about it. From the moment you have an organism, it might not even be the right trigger point. From the moment you want to roll that organism into a process, into an application, then those things need to be evaluated (emphasis added).

This segment reflects the difficulty of addressing safety concerns when these cannot be identified in advance, only *imagined*. The same researcher added later “that comes along with the responsibility thing. And the other thing is, if you think about those things and the risk, there are only two choices. *Either we create that organism, or we don’t*. So that’s the only thing, and those tests... will be in place once the organism is there” (emphasis added). This space between creating an organism or not, is where social scientists can help scientists to occupy, assisting them in developing awareness of the multiple choices and decisions present in their judgments and practices. This suggests a dichotomy of action that can only be explained by a lack of imagination when thinking about managing risks, narrowing down multiples avenues of actions into few. It is important to make visible the grey space between black and white and the wide range of choices and instruments for governance available. Nevertheless, discussions about risk and safety are part of wider questions about values and carry normative and epistemological aspects. It is difficult to broaden the discussion not only in the laboratory, but in more open spaces, like the workshop in Birkbeck College about biocontainment and biosafety,<sup>174</sup> where an STS analyst commented, trying to steer the discussion into values:

It’s not about how safe is a technology... [the question is] what kind of technology should we be pursuing? It’s a completely different question.

This followed another intervention from a panellist who commented that they would like to see a methodology for incorporating values in the assessments of new technologies, since these types of questions are difficult to settle. Biocontainment by governance works for xenobiology because it relies on a narrow conception of risk and imagination of uncertainty. The difficulty of knowing the implications of xenobiology was highlighted in a laboratory discussion when a researcher commended on the work of Dana and colleagues (2012), who suggest that risks of synthetic organisms are difficult to predict (see above), “It makes sense, but essentially, it’s like trying to fit a grey wall into a black and white box... By definition is

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<sup>174</sup> See footnote 59.

unsound.” I asked clarification, remarking the complexity involved. The previous researcher commented,

No, is a case of, the argument is closed as well. You want to know risk; it’s not acceptable risk, it’s not minimal risk, it’s not proven risk. Which makes it very black and white. And from the moment you make a kind of black and white proposition, the only way to prove there is no risk, is by testing every organism on every environment, on every combination, which is unworkable. And chances are most organisms, including natural ones, will fail that... It’s a great statement, it’s very appealing, but it doesn’t work.

Hence, discussions about risk can become trapped in epistemological discussions that may blur the capacity to act, as the researcher invokes a problem of induction.<sup>175</sup> It is then challenging to determine guidelines for action versus precaution and thinking about risk in ways that do not obstruct experimentation in the laboratory but neither leave questions about wider impacts unaddressed. The discussions in the laboratory seemed to suggest that scientists were concerned about the hazards of their work but were also aware that they did not have proper frameworks nor support for addressing them; this is where institutionally dictated practices need to be established, to shape behaviours in the long term. The question of biosafety and biocontainment is peculiar because the problem is defined in terms of the tools available to solve it. It is far from optimal to solve problems with the tools that created them. The problems that xenobiology may create (i.e., toxicity and environmental impact) are evaluated with the same tools that scientists use to make XNA-organisms a reality; it is necessary to broaden the set of skills of scientists, to include carry out different experiments in the laboratory, but also to incorporate wider epistemic and transdisciplinary elements in their work. Nevertheless, risks in xenobiology not only motivate discussions about environmental impact, but also health hazards, a concern present since the dawn of genetic engineering. Such categories can become mixed when discussing biosafety in xenobiology. A theme that emerged in my fieldwork is that scientists are currently doing *enough* to address potential ramifications of synthetic biology. In the workshop about biocontainment and biosafety in Birkbeck College,<sup>176</sup> a member of the panel commented that it should be considered that

Folks in academia that are doing basic research have significant oversight. Students are highly trained. They have to take health and safety training on an annual basis, they have to take radiation safety training on an annual basis, they have to take a biosecurity and biosafety training on an annual basis; they have to sign disclosures to what technologies they’re working on.

In the laboratory I studied the safety of researchers was taken very seriously. Scientists were encouraged to wear safety gear always when conducting experiments, including laboratory coats and disposable gloves; at times when I performed experiments (such as gene

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<sup>175</sup> Or the black swan principle: "all swans we have seen are white, and, therefore, all swans are white", before the discovery of black swans.

<sup>176</sup> See footnote 59.

cloning), the researcher who oversaw my work paid attention to my use of gloves and coat. Safety can also be seen as protecting experiments from the interference of humans, as a researcher expressed. Concern over safety extended to the type of reagents that the principal investigator of the laboratory chose, for example favouring the dye SYBR safe® rather than ethidium bromide (a carcinogenic chemical) for staining agarose gels with DNA, and the choice of formaldehyde-free stains for acrylamide gels.

Addressing risk in xenobiology goes beyond a concern in daily research, to becoming a formality. It requires to be institutionalized in laboratory culture and the wider ethos of xenobiology (and for that matter, most disciplines). In the third discussion with the laboratory (which focused on risk and responsibility) I presented to the laboratory the suggestion of Moe-Behrens and colleagues (2013: 7) of requiring that scientific articles include a section to report ‘risk and biosafety information’ (see **Figure 12** for details). During the discussion, I mentioned that the main aim of this reporting card was building the capacity to draw conclusions on risk and safety from a large pool of studies.

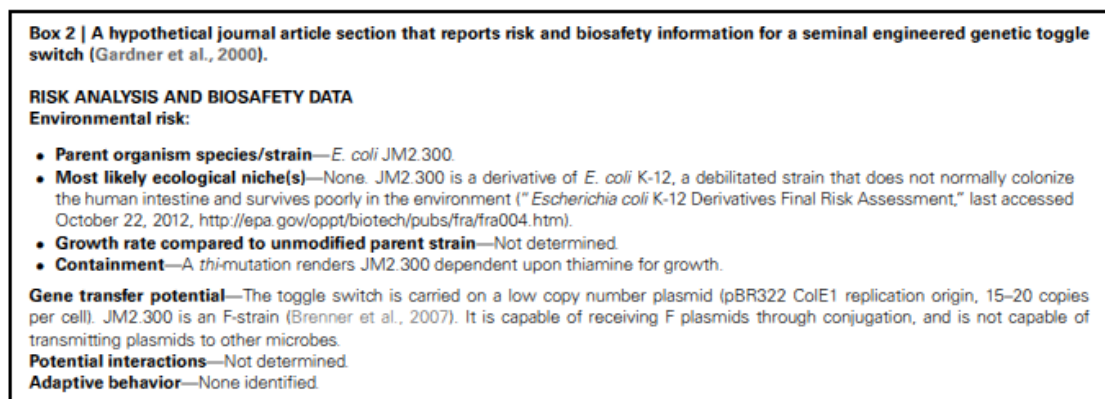


Figure 12. Suggested form to report data in scientific articles on risk analysis and biosafety (Moe-Behrens et al., 2013: 7).<sup>177</sup>

During the conversation that ensued about to the reporting of risk analysis data, asking whether it could be useful, a member of the laboratory commented, referring to safety data, that

*It will only ever be taken seriously if somebody gives scientists money to actually carry on the experiments, otherwise... if there is a big consensus on the researchers, the funding agencies, the journals, everybody has to be enthusiastic about it (emphasis added).*

This sentiment echoed a comment made earlier during the discussion: “Unless the [funding agency] gives me enough money to carry out those experiments, I’m not going to carry them out. It comes down to that.” The researcher added that conducting experiments needed for risk assessment is complicated, far from straight forward, and expensive. Such structural constraints for thinking about risk need to be addressed as they are part of the ‘rules

<sup>177</sup> This card references Gardner, Cantor, & Collins (2000).

of the game', the unwritten rules that influence scientific practice. How research is financially supported is a key piece of discussions on responsibility, since it dictates the type of research that can be conducted, and the attitudes that researchers adopt. Later in the discussion it became clear that scientists supported measures like examining and reporting risk data but were unsure about the type of institutional arrangements or norms that would enable that. It would require an additional set of duties and housekeeping that would lie beyond the scope of research that would lead to translatable results. Would this require the constitution of an oversight mechanism? How would it be overseen? At one point, a participant commented that similar guidelines to the reporting of quantitative PCR<sup>178</sup> data could be followed; this would maintain the autonomy of scientists over their research. In this context, reporting risk data would be performative, prompting scientists to consider potential downsides of their research, rather than ensuring that experiments were conducted under calibrated and reproducible conditions, which would be the aim of quantitative PCR guidelines, or even ancient DNA research guidelines. Nevertheless, oversight mechanisms in xenobiology would enable anticipation and agreement over risks, benefits, and purposes of research, rather than establishing quality control. If institutional structures do not support or incentivize mechanisms to take safety and 'unknown unknowns' seriously, it becomes difficult to commit researchers to fully anticipate negative consequences of their work. Scientists try to 'play by the rules' and adhere to the norms of their community.

Talking about risk because of its undefined nature, and epistemological limitations. This is problematic the difficulty of incorporating uncertainty in the governance of xenobiology is used as an excuse for inaction, or all the opposite, confidence in containment mechanisms is sufficient for considering these questions as resolved. Scientists are not keen about including risk themes in their agendas but are interested in preserving the structures that ensure their career progression and measurement of success, adhering to long-established norms. This co-production of knowledge and social order reflects how the current knowledge production regime shapes the type of questions that researchers ask that do not include aspects of risk assessment or negative outcomes, which are outsourced or stored for dealing with later on. This is connected to the notion of responsibility of scientists complying with a public perception of risk, designing safety features as a policy of managing risks: it ensures there is no need to do so. It is important to better understand how scientists approach risk and values, and whether differing ways of thinking about experimentation can result in different attitudes to these topics. I address this topic in the next section.

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<sup>178</sup> See Bustin et al., 2009.



## 7.4 A more experimental approach to risk assessment

I have pointed out difficulties and limitations for thinking about xenobiology in systemic terms, concerning the relation of organisms with their environment. The focus of scientists on engineering the properties of microorganisms that dictate their behaviour, and their reception by society, does not encompass the complexity behind the interactions of organisms with their environment. By this I refer to the difficulty of identifying and quantifying causal links between actions and outcomes, including interactive effects between agents (i.e. feedback loops), delay periods between cause and effect, and intervening variables (Renn, 2008). I approached questions about risk assessment and experimentation with the laboratory and interviewees as a vehicle to broaden the discussion about what is at stake with xenobiology and what topics deserve deliberation. Testing, as I showed above, is tied to institutional structures in place, including rewards and incentives for scientists, and the scope of research grants, which shape the responsibilities that scientists assume. Strategies and institutions for managing biological risk in emerging technologies have not made significant progress in the last 40 years since the birth of genetic engineering (Palmer, Fukuyama, & Relman, 2015). Ulrich Beck refers to a 'safety circle,' in which safety cannot be tested before artefacts are actually built and used,

We no longer find the progression, first laboratory then application. Instead, testing comes after application and production precedes research. The dilemma into which the megahazards have plunged scientific logic applies across the board; that is, for nuclear, chemical and genetic experiments science hovers blindly above the boundary of threats. Test-tube babies must first be produced, genetically engineered artificial creatures released, and reactors build, in order that their properties and safety can be studied. The question of safety, then, must be answered affirmatively before it can even be raised. The authority of the engineers is undermined by this 'safety circle' (Beck, 1992: 108).

As discussed in **Chapter two**, in the current knowledge production regime the boundaries between laboratory and society are less and less demarcated, where freedom of research means freedom of application (Krohn & Weyer, 1994). Researchers maintain power to establish what goals are worth pursuing, expecting that society should accommodate to new social orders. Biocontainment technologies are particularly relevant because in xenobiology this is aimed to allow the release of genetically engineered organisms into open environments, crossing an arbitrary barrier between the laboratory and society. The release of contained microorganisms can be seen as ecological engineering, impacting ecological processes and involving a different form of experimentation than the laboratory. Giving up the illusion of controlling life, considering lessons from real-world experimentation, clears our conceptual toolkit to think about novel experimental approaches to safety and release. The question is not only about experimentation but about platforms for deliberation. I return to this point after providing a brief overview of studies about gene drives that relate to the question of impact on ecosystems and complexity. Gene drives offer an excellent standpoint

to reflect on interventions that may affect entire ecosystems, so the questions they raise are relevant for xenobiology.<sup>179</sup>

Gene drive systems are a recently developed genetic technology that allows spreading genetic changes through a wild population even when such changes reduce fitness; because they can suppress populations by disrupting recessive fertility genes, they have been suggested as a solution for vector-transmitted diseases such as malaria or zika (National Academies Press, 2016). They are theorized to act in a similar fashion to invasive species, raising concern about their potential to spread further than intended, transforming entire ecosystems in unanticipated and unexpected ways (Esvelt & Gemmell, 2017). Gene drives are interesting because their potential to get out of control limits reliance on safety mechanisms for their governance, providing a useful mirror to think about safety and release in xenobiology. The emerging field has sparked discussions about responsibility in science, mainly led by gene drives pioneer Kevin Esvelt.<sup>180</sup> Ken Oye and colleagues (2014) provide an overview of the gaps for governance and regulation that gene drive technologies face. They recommend,

Adopting a function-based approach that defines risk in terms of the ability to influence any key biological component the loss of which would be sufficient to cause harm to humans or other species of interest. The agents and targets of concern with a functional approach could include DNA, RNA, proteins, metabolites, and any packages thereof (ibid., p. 628).

Still, they frame regulation and governance as matters of risk assessment and management and recommend ten steps for an integrated management of environmental and security risks. Of these, I highlight the reversibility of interventions, monitoring of gene drives in environmental samples, not testing in areas inhabited by wild species, and long-term studies. Noteworthy, they portray containment as a measure of management:

Investigations of drive function and safety should use multiple levels of molecular containment to reduce the risk that drives will spread through wild populations during testing. For example, drives should be designed to cut sequences absent from wild populations, and drive components should be separated (ibid., 627).

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<sup>179</sup> For a comprehensive discussion of the governance of gene drives, see the special issue of the *Journal of Responsible Innovation* (2018, Vol. 5, Sup. 1): "Roadmap to Gene Drives: Research and Governance Needs in Social, Political, and Ecological Context; Guest Editors: Jason Delborne, Jennifer Kuzma, Fred Gould, Emma Frow, Caroline Leitschuh, and Jayce Sudweeks." Available at <https://www.tandfonline.com/toc/tjri20/5/sup1> [Last visited 3 December 2018]. See also Evans & Palmer, 2018.

<sup>180</sup> See for instance Kevin Esvelt's initiative 'responsive science', accessible at the website 'Responsive Science; The 'about' section displays "responsive science is a way of conducting research that invites openness and community involvement from the earliest stages of each project. Real-time interaction between scientists, citizens, and broader communities allows questions and concerns to be identified before experiments are performed, fosters open discussion, and encourages research studies and new technologies to be redesigned in response to societal feedback." Retrieved from <https://www.responsivescience.org/about> [last visited 5 September 2018]. See also Eaves, 2018.

In gene drives, biocontainment is also promoted as a useful mechanism to ensure safety; studies have addressed its feasibility (Benedict et al., 2018; Marshall & Akbari, 2018; Quinlan et al., 2018). Remarkably, pioneers of gene drives have recognized the value of public participation and involvement in decision-making. A case in point is Kevin Esvelt's goal of employing gene drives in the island of Nantucket, Massachusetts, to control the spread of Lyme disease.<sup>181</sup> His plan involved using genetically engineered white-footed mice (vectors of Lyme disease) vaccinated from infection with *Borrelia burgdorferi* —the agent of Lyme disease— using gene editing to incorporate in mice antibodies known to combat the disease. In Nantucket there is a prevalence of Lyme disease of over 40%; as an island it is a well-suited geographically contained location to conduct an experiment with gene drives. Esvelt's approach has gained attention in the media for giving decision-making power to the local community. In an early phase of the project, Esvelt went to Nantucket and Martha's Vineyard to talk to residents and attend a town meeting. He explained the goals and strategy of the project and listened to the concerns and opinions of those potentially affected (or benefited). At the time of writing, the project has not received green light by the local community, and Esvelt respects their choice. If the community does not want to have a gene drive experiment to combat Lyme disease in their land, Esvelt is willing to walk away, rather than trying to convince them. For Esvelt, transparency is a key feature of what he calls 'responsive science', and a key to earn public trust. His attitude is remarkably similar to lessons of real-world experimentation (**Chapter two**); for instance, he commented:

Even beginning to do the work in the lab means you're making a decision that could affect people out of a lab ... For [a] gene drive, the closed-door model is morally unacceptable. You don't have the right to go into your lab and build something that is ineluctably designed to affect entire ecosystems. If it escapes into the wild, it would be expected to spread and affect people's lives in unknown ways.<sup>182</sup>

Nevertheless, engaging the public is not free of uncertainties (Rudenko, Palmer, & Oye, 2018). Rudenko and colleagues recognize the importance of public engagement but claim that as a process it needs to be effectively managed. Engagement exercises may bring back negative experiences or perceptions from previous controversies to new technologies like gene drives. The authors also bring attention to the need of developing capacity for testing and using gene drive technologies in regions that are associated with low scientific capacity, such as countries where malaria is endemic. This brings new challenges for engaging with communities that hold different worldviews and may not share the same assumptions and values about science in the Global North. A well-known recommendation for successful

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<sup>181</sup> See Yong, E. 2017. One Man's Plan to Make Sure Gene Editing Doesn't Go Haywire. The Atlantic. <https://www.theatlantic.com/science/archive/2017/07/a-scientists-plan-to-protect-the-world-by-changing-how-science-is-done/532962/> [last visited 6 September 2018].

<sup>182</sup> Ibid. Quoted in the article.

engagement is allowing the possibility of rejecting technological interventions and accepting that traditional approaches to solving problems may be preferred.

Esvelt's proposed interventions draw upon themes in the literature on governance of technology, such as trying possible alternatives (not necessarily based on cutting-edge technology) before deploying gene drives for solving a problem; for example, using bed nets or insecticide spraying for combatting vector-borne tropical diseases. In their reflection on engaging publics with gene drives (Najjar et al., 2017), Esvelt and colleagues emphasize on involving local citizens because they are likely to be aware of useful ecological information that researchers may not know or have access to.<sup>183</sup> The authors are also concerned with the *scale* of interventions, being aware that gene drives (i.e., in the case of genetically modified mosquitoes) do not distinguish boundaries between nations or territories and their potential to spread unwanted genetic changes is high. They advocate for local interventions, where specific ecosystems are geographically bounded, such as islands. Interventions in synthetic biology could be framed as being possible anywhere, without a specified context or delimitation, and research in gene drives emphasizes the importance of thinking that the (geographical) qualities and characteristics of each ecosystem are relevant. The case of gene drives and their deployment in ecosystems as a real-world experiment is a useful mirror to reflect upon responsibility and risk in science. Hence I introduced to the laboratory group discussions the 'scientific philosophy'<sup>184</sup> that Kevin Esvelt wrote for his laboratory a manifesto for conducting responsible research, that proclaims that scientists "must be mindful of our responsibilities to our colleagues, our funders, humanity, and the natural world." A segment of the text briefly illustrates Esvelt's approach to responsibility.

To humanity, we owe transparency and responsiveness. As scientists, we have a professional responsibility to share the possible consequences of our research with the public in an understandable manner. If our research will not have any such consequences, we're clearly doing something wrong. More generally, we must invite, listen, and respond to concerns as best we can.

Later in the text they adopt a consequentialist ethics perspective, placing the burden of scientific consequences on scientists themselves:

We are morally responsible for all consequences of our work. It does not matter whether our research is approved by an institutional biosafety committee, regulators, potentially affected communities, the International Association of Bioethics, or the National Academies. Moral responsibility cannot be outsourced: as we are likely the ones with the greatest knowledge of what might go right or wrong, the burden is ultimately upon our shoulders.

In alignment with the argument of this thesis, it shows hubris and confidence in scientists' control over nature. Researchers in synthetic biology should be more aware of uncertainty

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<sup>183</sup> This can be referred to as the importance of 'lay knowledge'; STS analysts have claimed the importance of understanding the plurality of knowledges and expertises that coexist in the world.

<sup>184</sup> See <http://www.sculptingevolution.org/philosophy> [last visited 6 September 2018]. See also Esvelt, 2016.

and acquire an attitude of learning from experiments, without assuming that full control can be achieved. Back to the laboratory discussion, I distributed printed copies of the text so the participants could read it. It prompted reflection and discussion in the group and various members either supported the statements or rejected them. Some members of the laboratory criticized the ‘scientific philosophy’ by being too idealistic and not committed to anything in particular. For them, the statements were sound, but were not binding. For example, a participant said “It’s a really well-crafted statement. But he promises nothing. It gives the impression of how they are gonna do things, [but] he makes no commitment.” Others claimed that as a philosophical statement, it should provide an ideal to aspire to.

The discussion in the laboratory exhibited that questions about responsibility and experimentation need to be considered in the context of the institutional structures that support and govern research. Institutional barriers, like those addressed in the previous section, must be considered when thinking about experimentation in different ways. A participant in the group (a graduate student) referred to the difficulties of fulfilling Esvelt’s ethos: “We compete with each other. At the moment that you have a system that funds research through grants, it’s competitive. So, you cannot say that I won’t compete with the other research groups, because you are always competing.” During the conversation, the point was made that Kevin Esvelt could *afford* to portray a vision of transparency, openness and care for nature. With the backing of MIT and a remarkable list of published papers, he does not have to worry as much as other researchers about competition or gaining grants.

Esvelt’s scientific philosophy and his approximation to responsibility in science (cf. Eaves, 2018; Esvelt, 2016; Najjar et al., 2017) displays a tension between placing the locus of moral decision-making on scientists themselves, as guardians of powerful research, while aiming to engage with publics as a way to earn legitimation. His reflection is appropriate but does not recognize sufficiently that different technologies bring different futures into being, different ways of valuing and relating to life. We need sophisticated frameworks for assessing risk such as *adaptive governance*, that “explicitly identify sources of uncertainty, accumulate relevant data to decrease uncertainty, and employ the accumulated evidence to inform subsequent actions or decisions” (Rudenko et al., 2018: 2). The release of gene drives, or xenobiological microorganisms, goes beyond an assessment of whether benefits outweigh risks. As such interventions involve all of society, they become discussions about values and the purpose of technological change. Recognizing this principle of technology governance, for ‘gene editing’, Sheila Jasanoff and Ben Hurlbut (2018) have proposed that the challenges of gene editing for humanity are of such magnitude that international oversight is required. They suggest the creation of

An entirely new type of infrastructure is needed to promote a richer, more complex conversation — one that does not originate from scientific research agendas but that instead

invites multiple viewpoints.” ... “a global observatory for gene editing, as a crucial step to determining how the potential of science can be better steered by the values and priorities of society (Jasanoff & Hurlbut, 2018: 436).

The global observatory would serve three purposes. First, centralize information and ethical and political postures from different groups, including civil society groups, and formal bioethics bodies, such as the Nuffield Council on Bioethics in the United Kingdom. Second, it would serve to track and analyse “significant conceptual developments, tensions and emerging areas of consensus around gene editing,” as well as a “a more detailed view of the biological futures people actually want for themselves and their societies” (ibid., p. 436). Third, the observatory would convey periodic meetings ensuring an international scope for discussions. Perhaps the greatest challenge and opportunity that such an observatory would face is widening the moral imagination of those who participate, making explicit assumptions and dominant views about humans’ control over life.

In this section I put together elements for further reflection on governance frameworks that embrace uncertainty, complexity, and lack of control. Concepts like collective experimentation and real-world experimentation provide useful lessons in this regard, particularly by erasing barriers between society and the laboratory, leading to the recognition that societies should have a say in the steering and evaluation of technologies. The result would be an agreement that we are all on the same side, facing the same risks, and bringing different values to the table. In the case of xenobiology, as the field is fuelled by imaginaries about life and society, its distance from implementation makes it difficult to steer the discipline. The fact that there are no previous cases to learn from makes decision-making difficult; dozens of cases of invasive species have been registered, along with their efforts to control them, but none with xeno-microorganisms.<sup>185</sup> Analyses must focus on interdependencies and spill-over effects that can potentially trigger impact cascades between otherwise unrelated components.

## 7.5 Summary and conclusions

In this chapter I reflected on the culture of risk assessment and experiment in xenobiology by drawing lessons from collective and real-world experimentation. Before providing an overview of the chapter, I will situate it in the larger narrative of this thesis. Having examined the imaginaries, visions and narrative that lead the development of xenobiology, the quintessential question about the ramifications of this emerging field remain: Are humans exceeding their mastery over nature? Are we as humans ‘unchecked’ when it comes to

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<sup>185</sup> See Davison (2005) for an overview of risks associated with the use of microorganisms for bioremediation.

imposing our will over nature? These questions, ever since Rachel Carson drove public attention in her book *Silent Spring* to the excesses of the chemical industry with the widespread use of pesticides, an awareness cannot be forgotten that scientists have the power to rewrite the way we live on Earth, and science can serve both to create artefacts and destroy nature. In this chapter I aimed to go one step forward, and while addressing themes of the (potential environmental) impact of XNA, I examine why such themes have not been settled, and new technologies raise questions of the unnaturalness of technology, human's alienation away from nature, and faith in technology to fix human problems.

In the first section of this chapter I draw attention to the materiality and scientific practice of xenobiology. The type of research that is conducted in the laboratory, in an individual basis, where biological systems are molecularized (**Chapter four**) and taken out of context, to be reconstituted under controlled conditions in the bench, makes it difficult to think and have conversations about ecological impact. Reductionism in the laboratory involves the types of questions that are asked, and also what researchers are expected to evaluate and investigate. If questions about undesired impacts of technologies are not brought to the laboratory, and reinforced through regulations, grant application requirements, and publication standards, it is difficult for new fields to advance in responsible ways. This realization about the reductionist character of xenobiology is important in order to highlight the importance of engaging with scientists, challenging their assumptions and co-constructing novel framings and narratives that are in tune with society's goals and ideals about nature.

In the second section I identify barriers for thinking about risk in xenobiology. I should clarify that I do not argue that risk is the main ramification to consider, but it is a relatable topic to introduce wider conversations with scientists about the consequences of their research. Through my engagement with scientists, I found that their priority is to 'play the rules' of the scientific institutions that dictate the terms for career progression and recognition by peers. At the moment, the advancement of xenobiology favours from developing biocontained microorganisms, but this takes for granted their safety for the environment; here, the language —or vocabulary— of biosafety (**Chapter six**) plays a role in the construction of an image of safety. Unlike nanotechnology, where the idea of 'safety by design' that Vicki Colvin elaborated captures that having more toxicological data about certain molecules allows to determine what properties/structures are riskier (i.e. causing cancer, or harming fish in standard toxicological tests) (Kelty, 2009), such a connection is absent in xenobiology.

The third section of this chapter was oriented toward recent developments in the life sciences that place challenges similar to those of xenobiology, especially when the release of

genetically modified microorganisms is considered. In this section I make the case of looking for frameworks for governance of xenobiology elsewhere, given the bias of xenobiology of embodying governance in organisms via design principles. As xenobiologists aim to release their genetically modified microorganisms in open environments, this raises questions ecological impact and the livelihoods of people in areas of intervention. The case of gene drives is interesting because its aims are similar in spreading organisms in ecosystems in a controlled manner. I analysed the approach of synthetic biologist Kevin Esvelt who has prioritized public participation and involvement in decision-making. I suggest that involving the public is important but not sufficient, since an epistemic tension of acknowledging or avoiding uncertainty needs to be addressed. An attitude of learning from experiments and mistakes and taking small steps without assuming that full control can be achieved, is recommended. We need sophisticated frameworks for assessing risk such as *adaptive governance*. Overall, such emerging fields —like gene drives or gene editing— bring along particular ways of thinking and managing their consequences; in other words, new technologies co-produce conceptions of responsibility and social value. For xenobiology, it is still early to tell what responsibility will be about, but it is safe to suggest that safety-by-design is not sufficient, and institutional mechanisms will play a major role. In the next chapter I provide a summary of the arguments presented in this thesis, along with the main contributions to the literature, and suggest next steps for continuing research about the limits that xenobiology may or not accept.



## 8. Concluding remarks

### 8.1 Approaching xenobiology from Science and Technology Studies

In this research, I set out to understand the work conducted to stabilize and position xenobiology as a field of safety. I explore efforts from scientists to redefine what counts as life and the boundaries between the natural and the synthetic. As scientists conduct efforts to rethink life, they also recreate discourses about how to fit new organisms into society, mobilizing a set of promises, narratives and discourses of legitimation. I place attention on *imagination* as being an essential component in the production of knowledge and technology; to what extent the role of imagination, imaginaries and visions shape the practices of scientists in laboratories has remained unaddressed in the literature. I study the emerging field of xenobiology, a discipline in the life sciences oriented toward the ‘exploration’ of the non-conventional biological world, through the development of alternative genetic systems. Xenobiology presents an opportunity that should not be missed to widen the range of actors involved in the discussion about values and imaginaries that technologies embody. Given rapid advances in the life sciences that cross unfamiliar territory, with breakthrough technologies for gene editing, cheap and efficient genomic sequencing, DNA synthesis, and other possibilities, it is relevant to study xenobiology as another vantage point from which to look the world-making potential of science and technology. In this concluding chapter I draw together the results presented in the earlier chapters and set them in the context of previous work in the field, providing a cohesive narrative of the research I present in this thesis. I make a contribution to the literature on ‘Science and Technology Studies’ and Governance of Technology, a public policy concept that refers to the steering between the sectors —state, academia, industry, and civil society groups— of the development of technology.<sup>186</sup> I also reflect on the methodology used in this research and collaborating with life scientists in order to promote reflexivity in the laboratory.

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<sup>186</sup> UNESCO defines governance (in a broad sense) as: “structures and processes that are designed to ensure accountability, transparency, responsiveness, rule of law, stability, equity and inclusiveness, empowerment, and broad-based participation. Governance also represents the norms, values and rules of the game through which public affairs are managed in a manner that is transparent, participatory, inclusive and responsive. Governance therefore can be subtle and may not be easily observable. In a broad sense, governance is about the culture and institutional environment in which citizens and stakeholders interact among themselves and participate in public affairs. It is more than the organs of the government...” Source: <http://www.unesco.org/new/en/education/themes/strengthening-education-systems/quality-framework/technical-notes/concept-of-governance/> [Last visited 23 September 2018].

This thesis is among the first systematic social studies of xenobiology, a branch of synthetic biology in the making. Researchers in xenobiology aim to show the field advances with responsibility, addressing from an early stage ethical and social implications that may arise. Efforts to promote frameworks of *responsible research and innovation* can benefit from a detailed understanding of the motivations of scientists and their own understandings of their duties toward society. As such, it is an excellent opportunity to study conceptions of responsibility in the community of life scientists. Xenobiology also offers a mirror that reflects how scientists think about the public and the type of values, prioritizing risk and safety, that are preferred. Last, xenobiology provides insights into how problems are defined and considered worth solving, and the type of solutions offered to address problems—in this case, biosafety. Biocontainment is a nail that the hammer of xenobiology can hit, echoing a comment from an STS scholar in a workshop.<sup>187</sup> The problem is not only having hammers hitting screws instead of nails, but the possibility of ignoring what the roots of the problems are in order to reach long-term solutions. The distinction between technological fixes and problems that technologies cannot address is not easy to make, but rather depends on institutional incentives, organizational structures, public policies, and the coordination of actors (Sarewitz & Nelson, 2008). How scientists determine worthwhile scientific problems, and what role imaginaries play (Macnaghten et al., 2005) is an important subject for RRI. In addressing solutions for biocontainment, we run the risk of not questioning why biosafety is needed, or what prompts it. The release of genetically modified microorganisms has been associated with possibilities for environmental clean-up of oil spills.<sup>188</sup> For example, Synthetic biology is offered as a solution to the worrying problem of oil spills,<sup>189</sup> but does not contribute to answering the question why such spills occur in the first place. Addressing environmental pollution with synthetic biology serves to accept a social order in which oil spills are accepted. Even though accidents in large-scale sociotechnical systems are unavoidable (Perrow, 1984), we could make a better use of emerging technologies by finding new solutions to problems, in conjunction with social rearrangements, rather than legitimize human-made problems. A field like xenobiology, following the commentator from the panel above, should aim to “do something useful, that can’t be done in another way.” For a richer discussion to be had, and more “socially robust knowledge”<sup>190</sup> (Nowotny et al., 2001) to be

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<sup>187</sup> See footnote 59.

<sup>188</sup> For instance, Ananda Chakrabarty’s oil-eating microbe was the first microorganism to be patented; see *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), was a United States Supreme Court case dealing with whether genetically modified organisms can be patented.

<sup>189</sup> For a discussion of alternatives to treat oil spills using microorganisms, see Biello, D. 2010. Slick Solution: How Microbes Will Clean Up the Deepwater Horizon Oil Spill. *Scientific American*. May 25. <https://www.scientificamerican.com/article/how-microbes-clean-up-oil-spills/> [last visited 14 October 14, 2017]

<sup>190</sup> See Weingart, 2008.

developed, it is necessary to broaden the scope of actors that participate in knowledge production, and allowing more of society to participate in the framing of problems that are subject to technical solutions. In a *Mode 2* regime of knowledge production, society needs to ‘speak back’ to science.<sup>191</sup> In the next section I provide a summary of the main points I make in each of the four chapters about results, along with the argument that connects them.

## 8.2 The cross-cutting theme of imagination and imaginaries

Imagination is a requisite for the engagement of publics in dialogue with technology-shaped futures and actors for the co-production of technoscience. Imagination is performative and has a collective character that can shape the frontiers of new disciplines. This thesis examines how researchers in xenobiology *reimagine* life, the type of imaginaries that support such moves, and corresponding ramifications into social and political arenas. Thinking about imagination invites exploring the narratives and rhetoric of xenobiology sought to legitimize a search for *limits*, to recruit support from other actors (i.e., government funding) to advance the research agendas of xenobiologists. The strategies that xenobiologists mobilize to associate their field with a responsible discipline, such as developing biocontainment, is among the main themes of this thesis.

Although the social aspects of xenobiology could be looked and written from different angles, imagination and imaginaries constituted the ongoing theme of the empirical results of this thesis. I started with the re-imagination of life that xenobiologists pursue (**Chapter four**) and analysing the narratives of xenobiology about life itself to deconstruct the proposition that the unnatural is the safer option (in biotechnology). Among the main points I argue is that using the heuristic device of *limits*, researchers in xenobiology aim to see what they can get away with when modifying life, testing what is biologically possible. In doing so, they redefine (and expand) the boundaries of life, to think of it as not exclusive of DNA-based organisms, decontextualized from an evolutionary history. Flattened engineered organisms, then, reflect that life is malleable, and could acquire many shapes, which does not make it less natural. Xenobiology then encapsulates an attitude to thinking and experimenting with life; these elements constitute to what I call the sociotechnical imaginary of *life unbound*. The extent to which researchers challenge established conceptions of life generates a need to justify research in the field. I argue that research accomplish this by

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<sup>191</sup> Nowotny and colleagues (2001: 117) They define socially robust knowledge as “[t]he reliability of scientific knowledge needs to be complemented and strengthened by becoming also socially robust. Hence, context-sensitivity must be heightened, and its awareness must be spread. The necessary changes pertain to the ways in which problems are perceived, defined, and prioritized, which has implications for the ways in which scientific activities are organized.”

expanding the boundaries of life, which in turns shift the rationales of biosafety. Proponents of xenobiology argue that risks are presented by DNA-based organisms. This discussion combines with the metaphors of navigation and exploring unknown biological worlds, because associating the unnatural with safety involves creating a separate space from the biological world. I suggest that these narratives should be understood as an effort of xenobiologists to create a niche (of built-in-safety) which only they can occupy, as well as attracting resources and visibility for their enterprise. In addition, exploring the limits of what is biologically possible results highly motivating for researchers. I finish by proposing that exploring life at its limits, expanding and redefining life, carries its own set of responsibilities, including knowing when not to cross limits, policing limits, and developing narratives that do not reflect domination and extraction of nature.

Continuing the exploration for limits, I take the standpoint that limits are also social, and xenobiology pushes the limits of what is socially acceptable, at the same time that it seeks to gain public trust and support. In **Chapter five** I study biocontainment (and design principles) as a form of governance, noting that achieving full safety can restrict the scope of deliberation and ethical issues, as other authors have also suggested. XNA-based biology acts as a tool of governance, justifying research in this area. I elaborate upon the argument that the 1975 Asilomar conference left a legacy of governance that has persisted through time, leaving a scientific agenda that shaped xenobiology. This matters because the narratives of xenobiology build upon existing ideas in circulation; scientists follow and continue the visions of predecessors to justify the agenda of xenobiology. I focus on the imagination of dealing with risks that determine the solutions that are sought: risks can be managed at the level of the organism. This relates to the sociotechnical imaginary of ‘controllable emergence’: controlling an organism, coupling responsibility and design, leads to management of public opinion. The 1975 Asilomar conference left a legacy of governance of a ‘challenge’ that can be solved in the laboratory, turning questions of governance into how to turn them into reality in the laboratory. Further, I argue that the imagination of managing risks at the level of the organism has downsides, such as ignoring the role of users and obviating the need for institutions, leaving matters of governance in the hands of scientists. Meanwhile, I highlight that biocontainment can serve other purposes of governance, like inscribing intellectual property protection features in genetically modified microorganisms, adding to the question of the framing of problems that deserve solution and the purposes of innovation.

Scientists produce knowledge that intersect with the society they live and work in, influencing the social configuration of the moment, which shapes the type of scientific practice they pursue. Continuing the discussion from the previous chapter, in **Chapter six** I

focus on the association of biocontainment with responsibility. I propose that scientists expect that design principles (of built-in-safety) will satisfy an imagined perception of the wants of the public, rather than addressing a scientific problem – what I call a technology of compliance. I show that there is no agreement in the scientific community on whether biocontainment is necessary,<sup>192</sup> so I argue it is a strategy to earn public trust and behave responsibly, because researchers must justify their research if their creations step out of the laboratory. In this sense, xenobiology needs protection from public backlash, the public must be contained. The second theme I address in this chapter is the version of responsibility as placing safeguards in microorganisms. This not only reflects an illusion of control of genetically modified organisms, but that researchers can frame problems and define what is biosafe, keeping their permission to continue experimenting. Zooming on the vision of not developing an XNA metabolism – a system to recycle XNA nutrients within cells, I argue that responsibility in biocontainment places too much emphasis on the producers of knowledge, putting at stake the distribution of responsibility allocated to users of technology.

Continuing the analysis of imagination in xenobiology, in **Chapter seven** I propose avenues for thinking about risk in xenobiology that embrace uncertainty –according to collective and real-world experimentation– and identify barriers in the laboratory culture that may impair such thinking. I make the point that the scientific practice of xenobiology is more reductionist than systemics, because in the laboratory, complexity is reduced; thinking of ecosystems and interactions between different species is not useful when the goal is to manipulate cells at the locus of the individual. In my fieldwork I addressed the potential environmental toxicity of XNA-related chemicals as a way to introduce questions about wider impacts. I discuss that the barriers for thinking and addressing externalities and hazards of xenobiology include also the lack of institutional support, i.e. funding and reward systems for incentivizing experimentation, and the contested nature of the limits of knowledge of risk. Lack of clarity about uncertainty leads to lack of action (or testing) in the laboratory. Then I suggest that uncertainty should be embraced, following frameworks of real-world and collective experimentation, that aim to erase barriers between the laboratory and society. This requires novel frameworks for governance, including ‘adaptive governance,’ the ability to anticipate unforeseen effects, and platforms for deliberation that draw scientists and society closer together.

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<sup>192</sup> Note that scientists do not agree on many issues, for example climate change, but due to a different set of reasons.

### 8.3 Studying sociotechnical imaginaries in the laboratory

The laboratory follows modes of ordering dictated by objects and relations between them (i.e. experiments) which reproduce certain patterns. The social can be understood as a materially heterogeneous ensemble of talk, bodies, texts, machines, enzymes, architectures, for which the laboratory provides a point of reference as an observer. It is a gathering space, where actors interact and produce meanings and transform objects and organisms. A place where discussions can be had. In my fieldwork, I approached the laboratory not only as the physical setting where xenobiological objects and organisms, were made, but also where a group of scientists shared and shaped among motivations, career goals, knowledge, values and above all, a shared identity as xenobiologists.

The study of the material and epistemological cultures of laboratories bring to the surface that, as Hess (2001: 240) puts it, “each society produces a knowledge about the world that encodes its cultural traditions even as it maps real structures and processes in the material and social worlds.” For Hess, a question for laboratory ethnographies is how cultural meanings and power relations are embedded in science and technology. Xenobiology presents a discipline (and case) representative of this tendency, with its concepts of biocontainment, biosafety, and second nature, to name a few, which carry meanings and properties that are *embedded* in genetically modified organisms themselves. Humans *delegate* (or translate) actions, work and disciplining to nonhumans (Latour, 1988a). Appreciating such delegation in the laboratory is fruitful but limited. What insights can the laboratory provide about the politics of xenobiology? What limitations I encountered while studying the lab?

Not all members of the laboratory I studied were aware about metaphors of xenobiology that pioneers proposed (i.e., *the farther, the safer*), though were working on projects that contributed to their realization, projects that were aligned with constructing built-in safety features. For example, even though participants would know Philippe Marlière because of his research and participation in conferences, for some members the agenda for xenobiology that him and others have envisioned was not known. I observed this in discussions in the laboratory, for instance in one occasion where I motivated a discussion on the ten design principles of xenobiology (Schmidt, 2010), to the surprise that some participants were unfamiliar to them. However, their research goals aimed to fulfil and achieve that design agenda, of isolating genetic systems. The discrepancy between not being aware of certain metaphors or visions, but conducting research related to them, is an interesting point of departure for further studies. In my fieldwork I was explained that junior researchers –like doctoral students or post-docs– do not have much room to determine the goals of their projects, sometimes they walk into already defined research projects. The focus for the

researchers, as I argue in this dissertation, is ‘making things work’, solving technical challenges and producing novel knowledge. In this sense, the cultural background of a research project, for example the rationale for biocontainment, seems to be lost in the process. In addition, this dynamic has to do with how researchers engage with the scientific literature, especially that which is filled with meanings and cultural references while referring to technical subjects – in other words, what literature they consume, and how they incorporate what they read into their own projects.

Second is the question of whether visions or ideals about the future are manifested and identifiable in the lab. They are sure incorporated in research goals and technological artefacts, but whether they are discussed and challenged is debatable. For sociotechnical imaginaries the future-oriented, world-building power of science and technology is among their main features; references to the future and what a *good society* might look like are absent in the laboratory. Some participants in the lab manifested their motivation to conduct science to build a better future (with better medicines, better biomedical tools), but these ideas were distanced from how xenobiological systems and organisms (with their inherent safety) could lead to the construction of a good society. The metaphors, visions and narratives that vanguards that xenobiologists put forward are not necessarily oriented to persuade and attract other (potential) xenobiologists, but can be seen as aiming to appeal the wider scientific community and public opinion, attracting visibility to the emerging discipline. In **Chapters five** and **six** I explained that biocontainment fits into a regime that favours the privatization of value in biotechnology, reductionism and control, based on built-in features. Even though such political ramification may not be evident for scientists, it is part of the job of the social commentator to bring these dynamics to the fore and ensure these aspects are properly debated and taken into account in the realization of xenobiology’s agenda.

It is open for debate whether it makes sense to employ the concept of sociotechnical imaginaries to study the political and social aspects of xenobiology, and whether the laboratory is a valid method to study this. What can we look for in the xenobiology laboratory and related actors, and what lessons can be derived for the concept of sociotechnical imaginaries at large? Sheila (Jasanoff, 2015b: 322-323) refers to four phases in the development of sociotechnical imaginaries: origins, embedding, resistance, and extension. I propose that this study is useful for the second and the last phases. *Embedding* is related to how sociotechnical imaginaries circulate and gain currency outside bounded communities. *Extension*, the last phase, consists of what allows imaginaries to spread across spread across cultures, boundaries, time and space. These questions must be examined in the light of the transition from a vanguard vision (Hilgartner, 2015) to a sociotechnical imaginary, once the vision has reached a collective character. My fieldwork in a xenobiology

laboratory gave me a magnifying glass to interpret the imaginaries and metaphors already in circulation, and the role that materiality plays in shaping and consolidating visions of the place of GMOs in the real world. Attention to materiality and experimentation is crucial to deconstruct metaphors and better understand the cultural resources they draw upon (such as a predominance of DNA as the molecule of life and evolutionary biology as a way of thinking about life, and the public as fearful of new technologies). Even though metaphors facilitate the understanding of complex ideas in reality, they are framed in biased terms. In this regard, the laboratory serves as a vantage point to understand the ideological content of sociotechnical imaginaries. The appreciation that ideas about safety and naturalness of genetically modified organisms enter the laboratory, and recruit institutional support, research funding and human resources can be taken as a sign of the collective character of the imaginaries that xenobiology mobilizes.

I show in this thesis that discourses, narrative and cultural resources about biology and society that xenobiologists mobilize, are not exclusive of xenobiology. Visions of the field, such as the unnatural as a safer option, or the legitimation of the release of GMOs (with their erasure of barriers between the laboratory and the real world by biocontainment) tap into imaginaries that suggest that the actual products of technology and design —GMOs— can embody governance and modes of association (Hurlbut, 2017b). The underlying theme that runs through this analysis and which is manifested in the laboratory, is whether safety and public acceptance can be achieved with more technology. In short, the influence and co-production of sociotechnical imaginaries with material culture and the sociotechnical arrangements they generate in the laboratory is indicative of visions that have achieved a collective status, at least within a scientific community. The ways in which biosafety is manifested and enacted in the laboratory reflects the context in which scientific work takes place, dependent on political regimes and cultures. Even though studying a laboratory cannot provide clues about how a sociotechnical imaginary rises from a vanguard vision to a collective status, through the analysis of experimentations and the practices of scientists, the laboratory helps to understand why a certain pathway is supported and becomes predominant. In other words, it helps to understand how material culture favours the adoption of particular sociotechnical imaginaries.

Another feature that helps understanding the dynamics of the laboratory and their relationship to sociotechnical imaginaries is *alignment*, the requirement of researchers in the laboratory to agree and build upon previous ideas and assumptions shared in a scientific community. Because the laboratory is not a place for the formation of beliefs or visions, rather a place for their consolidation, as this research shows, beliefs are a prerequisite for working in the laboratory. Some participants in the laboratory were not concerned about



biocontainment before joining the laboratory, but when they did, they aligned with a particular set of attitudes and goals in order to be successful in their research projects and ‘fit in’ with the culture of the laboratory.

As multiple sociotechnical imaginaries may compete with each other at a given time for a space in the collective imagination, the laboratory contains other imaginaries, by virtue of isolating, or delimitating, the outside world and its competing visions of what technology and its configuration in society could look like. Because experimentation is tied to a particular set of visions and promises of technoscience, researchers commit to a set of imaginaries, without necessarily questioning their origin or purpose. In focusing in making things work, or troubleshooting, they ascribe to a commitment that the unnaturalness as safe is the best path to pursue. The laboratory displays certain obduracy because its materiality helps to close down certain trajectories over others; for instance, in the case of the commitment an XNA metabolism, other possibilities and results are impaired.

In summary, I suggest that studying the laboratory with the analytical lens of the sociotechnical imaginary helps to understand the culture and motivation of researchers in a particular field and give resolution to the ideas that constitute those imaginaries. It is helpful to situate the phase of maturity (or extension) of sociotechnical imaginaries, for example in the case of biocontainment. Studying the laboratory allows researchers to gain a snapshot of a sociotechnical imaginary, with enhanced resolution, for a better understanding of its content and possibilities. Nevertheless, as much about sociotechnical imaginaries is about processes of change and adoption, which are better serviced by historical approaches, conducting fieldwork in different laboratories and ideally in different geographical locations, may offer a better chance of understanding the dynamics of sociotechnical imaginaries. Among the main motivations for this study for choosing the laboratory as a site of fieldwork was whether understanding the dynamics at play by sociotechnical imaginaries could lead to changing them, or steering them. I highlight that sociotechnical imaginaries circulate in the laboratory (at least in this particular case) in a ready-made form, where are adapted to ongoing practices and research goals; they are recruited with seldom questioning, leaving open questions for the STS analyst about how best to engage with scientists and understand their worldviews.

#### **8.4 Contributions to theory-building**

In this section I specify the main contributions for theory-building in the literature on evolutionary frameworks for governance of technology, including RRI, bioethics, and the growing body of literature on imaginaries in science and technology. I do so by bringing

attention to scientific practices in the (xenobiology) laboratory and the narrative, visions and discourses of safety that xenobiologists entertain. Moreover, I employ concepts from real-world and collective experimentation to think about control and uncertainty in xenobiology in the hope of providing foundations for a better governance.

#### **8.4.1 Expanding and supporting the engagement of scientists with responsibility**

RRI is an evolutionary meta-framework that aims to orchestrate existing mechanisms that broadly address responsibility in science and technology (Stahl, et al., 2013; Stahl et al., 2014). As an approach RRI builds on previously published work to support the governance of science and technology by enabling social learning and empowering social agency (Stilgoe, Owen, et al., 2013). It calls for the maximization of social and scientific benefits of research, calling for engagement with the context of its applications and challenges in the real world. In its core it aims for enhancing the reflexivity of researchers for anticipating potential impacts of the research, including the purposes and motivations of innovation. It also allows deliberation on uncertainties, assumptions and dilemmas about decisions that should incorporate a larger public than communities of scientists and innovators. RRI expects to turn the value-laden nature of technology into policy insights (Latour, 1992), its embeddedness socio-technical systems (Rip et al., 1995), and the need for interest for incorporating societal values (such as societal, ethical, political, legal, and environmental concerns) into practices of technology development (Grunwald, 2001; Hellström, 2003; te Kulve & Rip, 2011).

I propose that design principles in xenobiology not only involve forms of authority, but also capture ways of imagining responsibility and the public. Biocontainment is as a symbol of control over life which preserves an allocation of responsibility and authority over scientists to maintain their determination of what counts as risk, as safe, and as matters that deserve discussion in the emergence of the life sciences. There is more to responsibility than ensuring safeguards are in place. The observations I make in this study suggest the presence of structural constraints for embracing responsibility in a wider sense. Even though European science policy has made RRI a feature of its funding programs (i.e., H2020) and tackles what is perceived as a decline in public trust of science (Glerup & Horst, 2014; Zwart, Landeweerd, & van Rooij, 2014), attention needs to be paid to the forms of support, penalties and rewards that scientists receive for conducting responsible science. Funding and career progression schemes are overly focused on productivity and excellence, measured by various proxies like number of publications, collaborations, and citations. Researchers need the signal that the 'rules of the game' also include the opportunity to make mistakes, to change the direction of research projects, to evaluate effects that are not tied to the outcome, i.e. testing the toxicity

of XNA reagents in the environment when the goal is to produce a type of XNA molecular machinery. In other words, making the social norms and rules of the game less rigid and more conducive to thinking about responsibility. The culture of scientists who focus on the 'how' side of things (as in making things work), but never questioning the 'why' is still a topic of enquiry (Winner, 1990). It is especially challenging introducing to the laboratory what Winner calls *political imagination*: "the ability to envision the contributions of one's work to society as a whole, to the quality of public life" (ibid., p. 58-59). The recognition that technologies can enhance or diminish democratic participation, social equality, human freedom, and the public good. Partly because scientists experiment on problems that are already defined when they enter the laboratory (as in biocontainment) and because addressing such social considerations does not help advancing in producing publishable results.

Second, I argue that scientists aim to convey responsibility as built-in-safety features, ensuring *control* over the use of their artefacts or biological systems; design and engineering features are seen as the loci of action where scientists can intervene responsibly. I emphasize this association between control and responsibility by suggesting that a sociotechnical imaginary of 'controllable emergence' guides efforts in xenobiology. Relying on control draws from a consequentialist view of ethics, as researchers aim to avoid unforeseen uses or consequences of their research. This would work in theory if researchers were fully aware or knowable about the outcomes of their research. As I suggest, giving up control and embracing uncertainty is a vehicle to act responsibly, since it promotes a disposition to learn from mistakes and proceed with care. Moreover, such disposition would help to erase the abstract boundary between science and society and make more visible the role of publics in determining the trajectories of technoscience. Producing valuable knowledge earns a license to conduct research in the laboratory, free of moral considerations, as long as the research stays in the laboratory, as Francis Bacon defined his experimental philosophy (Krohn & Weyer, 1994).

This research also contributes to the importance of studying the purposes and motivation for innovation. Lorraine Daston (1995) refers to the moral economy of science as a web of values, held by collectives, highlighting that scientific practice is also influenced by normative, emotional, and aesthetic elements. Unlike Mertonian norms, they are rooted in cultural forms, and are particular to specific times and places. The goal of exploring life at its limits is not recent, as Langdon Winner remarked in 1990: "it now appears possible to renovate the genetic structure of life forms on the planet. But why? In what sense are such projects needed?" (Winner, 1990: 60). This goal has been accompanied by questions about the safety of genetically modified organisms and their impact on the environment. I suggest

that while scientific curiosity is a strong motivator, and scientists are driven by doing what no one else has done, and testing whether life can be modified in previously unknown ways, the justifications for a research area involve a wider set of considerations. The mechanisms and principles that enable biocontainment can serve other purposes such as increased intellectual property protection (at the level of the organism), or access to non-scientific actors (as in DIY-bio); these possibilities are not necessarily negative, but it is important to have an open and transparent dialogue about what biocontainment enables—or other forms of technological design and development—asking fundamental questions such as who will benefit and access the technology, how they may disrupt existing forms of production and labour, and their effect on democratic processes. Part of the challenges that technologies of containment bring is the possibility of neglecting conversations about the purposes and motivations for research, by providing an illusion and symbol that ‘everything is under control.’ The relational aspect of technologies and the sociotechnical systems that support them cannot be sidestepped with technology. In this regard, my research highlights the collective nature of the framing of problems. Goals such as biocontainment or the increased efficiency of intellectual protection work insofar other actors (i.e. decision-makers, research funders) share a common understanding of the problems that can be tackled through technology. Attention should be extended to other actors as holders of responsibility and participants in technological trajectories. The literature on STS (and RRI) has focused extensively on what happens inside the laboratory and discourses and narratives from policy makers. More research is needed to understand the dynamics of signalling of framing of problems and goals between different actors in innovation ecosystems.

#### **8.4.2 Imaginaries are built on previous existing resources**

The laboratory, as a place where expectations are formed and imaginaries are shaped, provided an excellent ground to observe ‘xenobiology in the making.’ It is in the laboratory where expectations can be reframed and sociotechnical imaginaries made visible (Gjefsen & Fisher, 2014). The laboratory is a site where power is concocted but its manufacturing is silently executed. If sociotechnical imaginaries draw attention to imagined forms of social life and social order reflected in the design of technological projects (Jasanoff & Kim, 2009), one aspect to highlight is the lack of heterogeneity of visions in the laboratory. In the laboratory I studied, biocontainment was established as a challenge to solve that required that members of the laboratory agreed on its necessity. Once it was accepted, few conversations questioned its articulation or its relevance, the question being ‘how to get there’ and manage the technical difficulties that arose during the process. For Sheila Jasanoff (2015), places to look for sociotechnical imaginaries include discourses and narratives. The

imaginaries I have described are reflected in texts that aim to attract attention to the field of xenobiology. Noteworthy, the sociotechnical imaginary of ‘life unbound’ incorporates elements of a technobiological imaginary in Fujimura’s terms, epistemic tools for the representation of nature; seen from the narrative that the unnatural is the safer option (**Chapter four**), the imaginary of ‘life unbound’ and exploring the limits of what is biologically possible imply configurations about safety and the introduction in society of ‘life as we don’t know it.’ More than studying the manufacturing and diffusion of imaginaries, the laboratory is a site where imaginaries are materialized, where visions and conceptions about life are inscribed in molecules and biological systems.

The design principles that reflected the imaginaries I have described, as well as a vision of governance-by-containment that Ben Hurlbut (2017), shaped research in the laboratory I studied. These imaginaries have turned into problems (or challenges) that can be addressed with technical means, in the laboratory, the result of hard work. A case in point is the design principles proposed by Markus Schmidt (2010) according to which an XNA metabolism should not be developed, in order to maintain the logic of biocontainment. Nevertheless, once these principles permeate the laboratory and find their way into research projects, the visionary baggage they carry seems to be lost. In the laboratory, researchers knew who Markus Schmidt or Philippe Marlière were, but the majority were unfamiliar with the metaphor of navigation new biological worlds that they propose. How visions, narratives and imaginaries turned into doable problems in the laboratory is a major question that this research leaves partially unanswered. It seems that goals, such as developing enzymes that work with XNA, circulate more easily than the rhetorical devices that support them and give them weight. The success of translating a set of visions and imaginaries, such as that the unnatural is the safer, and the value of exploring alternative possibilities of life, rests upon the use of already established cultural resources in the life sciences. As I show in **Chapter four**, much of the discourse around the imaginary of ‘life unbound’ comes from ideas of evolutionary biology, displacing the cultural predominance of DNA as the molecule of life, and the notion that real risks are caused by DNA-based pathogens. This matters because even though the ambitions of xenobiology of creating a *second tree of life* can seem transgressive, in practice they abstract patterns and habits of thought already in circulation. This not only suggests that xenobiology is not so novel, but that cues for what new technologies may bring are already present in cultural manifestations surrounding us. Related to this discussion is whether the imaginaries I have described, particularly that of ‘life unbound’, do point to a particular configuration of future worlds. Do proponents of xenobiology envision social change? The agenda of xenobiology does not convey a particular ordering of society, but the principles of biocontainment and its association with

responsibility do entail configurations of institutions (such as intellectual property protection) or the role of scientists in society.

So far, I have assumed a collective character of the imaginaries I have presented in xenobiology. Stephen Hilgartner (2015) suggests that we should first think of vanguard visions, which when sufficient work by leaders who assume a visionary role is conducted, and accepted by larger collectives, can become imaginaries. Most of the narratives, visions and metaphors I have presented in this thesis, which form the bulk of the sociotechnical imaginaries I introduced, come from a handful of *sociotechnical vanguards*, like Philippe Marlière, Markus Schmidt, or Victor de Lorenzo. The ideas I have presented come from more than a close-knit community. My intention has been to show that even though ideas come from few researchers, the materiality of such ideas transcends to a much larger community of xenobiologists, that includes research funders; how imaginaries travel and adapt to local contexts is a key question in this area. I attribute such success in spreading visions, such that the unnatural can be safer, because they build upon already existing cultural resources in the life sciences, as I explain above. Even though metaphors of exploration do not seem to propagate in the xenobiology community, underlying concepts that construct a discourse of safety do, and are mobilized by various actors. Remarkably, the vision of biocontainment of xenobiology is the realization of a path set forward as a result of the 1975 Asilomar conference, and xenobiologists capitalize on their unique capacity to fulfil this dream: genetically engineered organisms that cannot escape and can be biologically contained.

Another avenue of inquiry is what could be considered provoking (if not outlandish) narratives of proponents of xenobiology, or inflammatory, as one interviewee commented. 'Accepting no limits', exploring 'life as we don't know it,' or constructing a 'second tree of life,' as I have explained, can be seen as transgressive, defying a delicate balance between humans and nature. It is prone to agitate controversy. Similar to the performative role of expectations, visions and narratives carry meanings and modes of organization, prompting particular behaviours and modes of action. We should not only analyse their content, but how they are mobilized and for what ends. In a highly competitive environment such as the life sciences, where new areas of research sprung periodically, and opportunities seem endless, it becomes more difficult to signal to funders and peers that an area of research is more appealing than others. Following Latour and Woolgar's cycle of credibility, the narratives of xenobiology work to produce visibility (and capital) that is converted into grants, prestige, and production of knowledge (Latour & Woolgar, 1982). I found no evidence to support that other researchers were persuaded by such narratives and visions, but it was clear that the essence of exploring limits and questioning the foundations of life

seemed extremely appealing. Likewise, the character of the narratives creates a need for legitimization and public acceptance, especially as one of the goals of xenobiology is to enable the release of microorganisms in open environments. Hence the work conducted to portray xenobiology as a safe discipline, and the one that can best do the job of fulfilling the ideal of biocontainment sketched after the Asilomar conference. The strategies to seek legitimization, which reflect a sociotechnical imaginary of ‘controllable emergence,’ obey the rationale that control can be incorporated at the level of the individual (the microorganism) and the public, fearful of scientific creations spreading out of control, want contained spaces for experimentation. In summary, this research suggests the need to think about an ecosystem of narratives, mobilized and maintained by different types of actors, sustaining certain configurations of science and society.

### **8.4.3 Rethinking values and imaginaries in the life sciences**

This thesis seeks to re-open new paths for thinking about the life sciences. Xenobiology offers opportunities to rethink what is valuable about nature and our place in the world, including the way shifting definitions of life affect subjective experiences of selfhood, and our relation as humans to what is nonhuman. Establishing the novelty of xenobiology (and its politics) and its potential ramifications is only a part of this endeavour. I have suggested that the scientific practice and modes of experimentation in xenobiology are remarkably similar to those of molecular biology, which have been studied in depth in previous studies (see **Chapter two**). In drawing attention to the framing of problems in xenobiology, I have incorporated historical narratives and ways of thinking about the life sciences; this poses the question, what could have been asked since the beginning of genetic engineering that was left unasked or made invisible? Or does xenobiology offers an opportunity to re-open debates about the role of biotechnology in society? What alternative framings for xenobiology are possible? Even though I aimed to co-construct novel meanings and perspectives about the future of xenobiology with the researcher I engaged with, such hope was not fulfilled given the reasons I have already explained, including asymmetries of power, and structural constraints. Nevertheless, this research contributes to the understanding of narratives in xenobiology that can support strategies for re-thinking imaginaries in the life sciences. Synthetic biology faces pressure to translate research into commercial applications, and provide technofixes for humanity’s challenges, like the global food supply or renewable energy. Such inclination towards industrial applications can impair important conversations to be had about the role of technology in society.

Xenobiology could provide an opportunity to gain the terrain lost after the Asilomar conference as a missed opportunity to incorporate values into what became a technical

discussion about risk in genetic engineering and engaging a broad audience in biotechnology decision-making. Shobita Parthasarathy (2016) suggests ideas for developing a governance framework for CRISPR/Cas9 that also apply for xenobiology. An option for her is regulating biotechnology on the basis of moral and socioeconomic concerns, she gives the example of the pan-European patent system that prohibits patents on human embryonic stem cells. Second, she suggests incorporating public expertise in decision-making and framing of research in biotechnology, as I have addressed in **Chapter seven**. In opening alternatives for xenobiology, it is necessary to decouple the research agenda of the field—that is, its goals and expectations—with its justifications. Simply put, in thinking about the XNA molecular machinery, regardless of whether this is achievable, we should establish platforms for deliberation on whether this is desirable and acceptable for society. The research conducted today conduces to arrangements of society in the future, and the values and assumptions that guide the process deserve scrutiny. For instance, in drawing lessons from ‘Genetic use restriction technologies’ (**Chapter six**) I highlighted the proclivity of xenobiology to concentrate the suppliers and the sources of production of XNA-based supplies in ways that could resemble monopolistic behaviour. This is relevant not only for avoiding controversy, but for alignment with the goal of developing technologies broadly useful in society and accessible to most.

I suggest that xenobiology can offer an opportunity to engage and encourage the participation of actors from different backgrounds, in discussions about the means and ends of biotechnology, and the societal outcomes of research. Along with the incorporation of principles of accessibility, transparency, and accountability, opportunities would be open in terms of earning public acceptance of the field, the implementation of a culture of responsibility and relevance in science, increased support in terms of funding and infrastructure, and improved reputation for researchers in xenobiology. These themes come down to whether xenobiology can be *democratized*; by democratization I mean broadening access across the levels at which priorities are set. Features of democratization of science include extending user communities in reviewing funding applications (‘extended peer reviews’), community-initiated research where priorities emerge from the bottom up, and bringing closer interventionist-collaborative approaches (i.e., ELSI, RRI) to decision-making circles (Funtowicz & Ravetz, 1993; Guston, 2004). The democratic shaping of technology requires more than the input of citizens into technology outputs, to encompass reflexive and institutional changes both in scientific communities and civil society (Brown, 2006). Public engagement complements these processes, allowing a better management of uncertainties in science, holding the exercise of power accountable, and inquiring about the motivations and rationales for scientific research (Stilgoe, Watson, et al., 2013; Stirling, 2008, 2012).



The democratization of xenobiology requires expanding the range of actors that can access the technology and contribute to the field, in terms of producing and adopting scientific knowledge, and providing points of view. I propose two aspects that need consideration when it comes to future developments in xenobiology. Many xenobiologists develop applications not necessarily related to biocontainment, including the development of novel therapeutics and diagnostics, construction of nanostructures, and enzymes with novel capabilities (**Appendix one**). Notwithstanding, the goal of isolating genetic systems by artificial means (i.e., developing the XNA metabolism,<sup>193</sup> **section 6.3**) presents a commitment to a specific (linear) technological pathway. In sociotechnical processes, lock-ins are not desirable partly because they concentrate power in a reduced range of actors, limiting potential benefits of a technology, and impairing innovation and its social benefits. For xenobiology to become more than a tool for the management of intellectual property protection or restricting access to users, alternative pathways need to be developed. Currently, xenobiologists are pursuing various fronts, in terms of engineering the genetic code (even increasing the number of nucleotides in a codon to four, as Jason Chin's research group has accomplished), incorporating non-natural nucleotides in cells, and engineering proteins with artificial amino-acids. In order to create a rich ecosystem of possibilities, in terms of scientific knowledge and resulting applications, different approaches need to be developed independently. For this This requires broadening of the commitments to biosafety, and engagement in debates with actors with different stakes about the motivations for xenobiology and how the field can serve society.

According to Michel Callon (1994), flexibility, the support of multiple reconfigurations of technology, is a key property of sociotechnical systems, which markets tend to diminish. Lowering the costs and barriers of entry to research in xenobiology is important if the field is to be open and responsible. I show in this dissertation that research in xenobiology is costly, projects can cost millions of British pounds. In addition, research requires sustained efforts over time, to construct and refine xenobiological systems (often from scratch). This owes to a variety of reasons, which include the technical difficulty of manufacturing non-commercial artificial reagents, for example, XNA nucleotides and non-natural amino-acids, and the tacit knowledge required. In short, a sociotechnical network has not been fully developed around experimentation in xenobiology, which can take time, depending on the

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<sup>193</sup> The notion of XNA metabolism consists of the production and metabolization of XNA materials with biological systems, instead of chemical synthesis. An XNA Metabolism would require the development of certain features so that cells can 'recycle' or break down XNA nucleotides (or artificial amino-acids) and incorporate them in other cellular processes, for example to produce energy, or primary metabolites like carbohydrates or lipids. This is a principle suggested by Markus Schmidt, who wrote "Natural organisms must also not be able to produce these essential biochemicals, to avoid a symbiotic relationship with XNA." (Schmidt, 2010: 328).

promises and results that researchers fulfill over the coming years. Overcoming these barriers for entry requires a coordinated effort between xenobiologists to make reagents and techniques in xenobiology more cost efficient and accessible, as part of a culture of openness and transparency. A particular challenge is presented by issuing patents on products of xenobiology, which might elevate the cost of reagents and protocols, restraining the range of researchers that can contribute to the field. If that is the case, important discoveries could be missed, along with the input from actors with particular interests that might be neglected, for example the development of drugs for neglected or tropical diseases. In summary, flexibility depends partly on whether xenobiologists opt for steering their field toward a culture and regime of openness (cf. Calvert, 2012; Oye & Wellhausen, 2009). As I show, such cultural shift is restricted by the sociotechnical imaginaries that guide the development of xenobiology, especially which favor control (and biocontainment) as a form of responsibility and ordering.

## 8.5 Future steps

Being creative about alternative imaginaries, narratives and visions for xenobiology also entails creativity in engaging with scientists to articulate and disseminate them (see **Chapter two**). From my experience, doing so requires more commitment in the laboratory in terms of time and resources. Scientists are usually busy conducting experiments and activities that would lead to the production of knowledge, so for them to set time aside to think about social and ethical aspects requires additional effort, including the mandate of the principal investigator and the valuing of investing time in these activities. It would have been ideal to have more time to conduct lengthier workshops with the laboratory, for instance in which scenario-planning could be addressed. It is difficult to look back to evaluate the impact I had in the laboratory I studied. The projects that were in place were not altered because of my participation, and the laboratory did not establish plans for a comprehensive risk assessment of ecological impact of XNA reagents. But my presence and interactions with the xenobiology community might have effects that are not tangible, in the sense of seeding questions and awareness about the ramifications of scientific research for society. Through discussions in laboratory group meetings, chats while conducting experiments, and conversations over coffee breaks in academic conferences, I acted as a signal that there are conversations that need to be had with a wider public. The principal investigator of the laboratory once told when talking to him about RRI I was ‘preaching to the converted.’ I hope the ideas we discussed will have a lasting effect in this research agenda, and the wider agenda of xenobiologists.

In a qualitative study of this magnitude, I identify aspects that I would have handled differently with the benefit of hindsight. Given the limitations of funding and the scope of the project, it would have been valuable to conduct workshops and events that combined researchers in synthetic biology and researchers from various backgrounds (i.e., social sciences, theology, policy) with a focus on governance and ethics. The events where I participated were mainly about the science behind synthetic biology, with few opportunities to engage in discussions about the ramifications of xenobiology. Had the opportunity existed, I would also have liked to conduct meetings (i.e., focus groups) that allowed the interaction of researchers in xenobiology with lay publics, as spaces for exchange of perspectives on the topic. I have argued in this thesis that the framing of xenobiology is too far from public needs, in part due to a self-imposed distance between scientists in the laboratory, and society.

The research presented in this thesis is anchored in a comprehensive body of literature in STS, ethics of science and technology, governance of technology, and science policy. However, part of its novelty lies in studying the emerging field of xenobiology, opening questions that can be addressed in future studies. It still remains to be seen if xenobiology grows to be a dominant field in the life sciences, earning a place in the media and debates about ethics, as the case of gene editing, which has earned the spotlight. To the extent of my knowledge, a third xenobiology conference is not being planned, putting into question the momentum that the field gained. Still, much can be gained from studying xenobiology as it profoundly concentrates tensions and disputes over what problems are worth solving through technology, and a continuation of the unsettled issue of the place of genetically modified organisms in industrial societies. The research presented in this thesis could be complemented by reaching a more diverse set of actors, to include not only scientists, but lay publics, decisionmakers, and civil society members, either through interviews or focus groups. This is limited by the extent to which xenobiology is known by actors, as I explained in **Chapter three**. Also, of interest would be to conduct comparative studies of laboratories that conduct xenobiology-related research in the U.S. and Europe, to determine the extent to which different political cultures influence the narratives of xenobiology. The work I present does not fully distinguish between the geography of xenobiology, due to its exploratory nature. Even though the narratives I present are mainly articulated by European actors, the foundations of the narratives and imaginaries, as I argue, are drawn from cultural resources in the life sciences. Speaking of comparisons, it would also be useful to compare xenobiology with emerging fields like gene drives (**Chapter seven**) and protocell research (cf. Bedau & Parke, 2009), as they share competing goals of reconstructing life in the laboratory as well as disseminating engineered forms of life in ecosystems. On a separate note, xenobiology challenges existing regulatory frameworks and shakes deeply held views about the order of nature and the place of humans in it. Studies that address the making of regulatory

innovations for the life sciences —including the release of genetically modified organisms or their impact for biodiversity and international trade— and the making of financial instruments (like grants) will add plenty to the picture of xenobiology gaining a place in society.

In the years to come, developments in the life sciences (and xenobiology) will continue to surprise us and shake the foundations of different cultures around the world. I hope to have positioned xenobiology as a useful subject of study for understanding responsibility in science and establishing governance frameworks that incorporate reflexivity in scientific practice and lead to scientific developments that better suit the needs of society and are sustainable for the environment.

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## Appendix 1: important developments in xenobiology

This appendix provides background on xenobiology, in terms of the history and origin of the field, which I address in the first section. I show that since the beginning of molecular biology, scientists have been interested in modifying the genetic code, and experimenting with novel types of nucleic acids.<sup>194</sup>

The imagination that the genetic code or the chemistry of the genetic system could be different is as old as early efforts in molecular biology following the discovery of DNA as the molecule of heredity. In 1962 Alexander Rich proposed the possibility of an artificial, third base pair between isoguanine (isoG, 6-amino-2-ketopurine) and isocytosine (isoC, 2-amino-4-ketopyrimidine) (Rich, 1962; cited in Hirao & Kimoto, 2012). Arthur Kornberg, one of the most famous biochemists, known for the discovery of the mechanisms for DNA synthesis and replication (cf. Friedberg, 2006) used non-canonical nucleic acids in his experiments<sup>195</sup>. As a side note, Arthur Kornberg's announcement of the synthesis of biologically active DNA was misinterpreted in the news as he had 'created life in the test tube,' sparking controversy at the time about the ethics of molecular biology (cf. Kornberg, 1989: 200-204). In a parallel note, experiments conducted for elucidating the genetic code also involved manipulation of tRNAs, which were altered to insert "incorrect" amino acids at certain positions in proteins, creating useful mutations, that lead to an ambiguous code generating variable products and inefficient protein production (Kaplan, 1972).

Steven Benner is a pioneer of the study of DNA analogues. As Roberta Kwok (2012) reports for *Nature*, Benner was surprised in the end of the 1970s because organic synthesis of natural products was in vogue, but no one paid attention to DNA. In Benner's words, "[c]hemists were looking at every other class of molecule from a design perspective except the one at the centre of biology" (ibid, p. 516). Benner's work initially focused on unnatural

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<sup>194</sup> For reviews on discoveries related to xenobiology, see Acevedo-Rocha, 2016; Acevedo-Rocha & Budisa, 2016; Brudno & Liu, 2009; Chaput, Yu, & Zhang, 2012; Hirao, 2014; Hirao, Kimoto, & Yamashige, 2012; Hoesl & Budisa, 2012; Malyshev & Romesberg, 2015; Pinheiro & Holliger, 2012; Pinheiro, Loakes, & Holliger, 2013.

<sup>195</sup> Articles by Arthur Kornberg were discussed in a laboratory meeting of the group I followed. In my field notes I wrote that such non-canonical nucleic acids were used for convenience, since they had functional groups attached (like fluorescent molecules). The presenter of Kornberg's papers explained later that she was interested in such historical perspective because Kornberg's group at the time were facing similar problems to the ones the laboratory currently faced, and Kornberg's solutions proved creative and effective.

nucleotides pairing via hydrogen-bonding. His lab reported tested two unnatural base pairs, *iso-C* and *iso-G* (Piccirilli et al., 1990; Switzer, Moroney, & Benner, 1989) which could be read by DNA polymerases, but the bonding was unspecific, and *iso-G* tended to pair with T, instead of *iso-C*. In 1992, Benner's lab accomplished a new technology for incorporating non-standard amino acids into polypeptides, using an in vitro ribosome-based translation system with the unnatural base pair isoG–isoC, for the site-specific incorporation of a non-standard amino acid, 3-iodotyrosine, into a peptide, by creating a new isoCAG codon (Bain et al., 1992).

Parallel developments took place by one of Benner's competitors and pioneers, Eric Kool, who studied unnatural base pairs that paired without hydrogen bonds. His lab developed an analogue of the nucleotide Thymine, called difluorotoluene (designated F), by replacing fluorine for oxygen atoms. 'F' does not pair with the nucleotide Adenine via hydrogen bonds, but polymerases recognize it as Thymine. This work showed that hydrogen bonding is not as important as previously thought, highlighting the importance of hydrophobic properties of DNA chains.<sup>196</sup> Efforts to expand the range of DNA-based nucleotides (or letters) have been progressive. These include base pairs that form stable parts based on interbase hydrophobic interactions, instead of hydrogen bonds, and have been found to be recognized by DNA polymerases (Wu et al., 2000).

Two other pioneers in the study of unnatural DNA are the laboratories of Ichiro Hirao and Floyd Romesberg, that have focused on using hydrophobic and packing forces to control the pairing of unnatural base pairs. Hirao, a chemist at the RIKEN Systems and Structural Biology Center in Yokohama, Japan, developed an interest creating unnatural bases from reading James Watson's 1968 book *The Double Helix* as a teenager (Kwok 2012). He started in 1997 by testing Steven Benner's hydrogen-bonding geometry concept with steric hindrance effects (Hirao & Kimoto 2012). Whereas Hirao has focused on 'shape complementarity' analogues, similar to natural DNA base pairs, Romesberg has studied nucleic acids without taking into account their shape (Feldman & Romesberg, 2018). In 1999, Romesberg's group reported successful hydrophobic self-pair between the 7-propynylisocarbostyryl (PICS) bases in single-nucleotide insertion experiments (McMinn et al., 1999). In the 1990s researchers focused on studying in further depth the properties of DNA-based unnatural base pairs; shape complementarity between nucleotides and the strength of hydrogen-bonding interaction affected base pair formation (cf. Hirao et al., 2002); further questions in the field have been the recognition of unnatural base pairs by polymerases (Eom, Wang, & Steitz, 1996; Morales & Kool, 1999). However, in the 1990s difficulties found in hydrogen-bonded unnatural base pairs slowed down interest in the field. Overall, three families of unnatural

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<sup>196</sup> See Moran, Ren, & Kool, 1997; Schweitzer & Kool, 1995.

base pairs have been developed: dZ-dP, developed by the Benner laboratory, dDs-dPx, developed by the Hirao laboratory (Kimoto et al., 2009), and dNaM-d5SICS, developed Romesberg lab. These efforts have resulted in amplification by PCR of unnatural DNA with high selectivity (cf. Hirao et al., 2007; Malyshev et al., 2009; Yang et al., 2011). Sismour & Benner (2005) reported the use of thymidine analogues to address the problems of tautomerism problem of isoG, which lead to infidelity in PCR replication.

The process for selecting unnatural base pairs requires tweaking the organic chemistry of DNA. It is based on ‘proof of concept’ experiments, of which a first step is the design of unnatural base pairs changing (Romesberg lab has used a process involving thousands of combinations, a drug discovery approach). The nucleotides are chemically synthesized, which can be tedious and supposes challenges for providing enough quantities. Third, replication and transcription using the unnatural base pairs and DNA templates are tested in vitro. Problems found at this stage are reincorporated into the design process, creating a cycle, until suitable base pairs are found that can be used in replication, transcription, and/or translation systems. Such experiments have benefitted from the engineering of DNA polymerases and automated DNA sequencers (Hirao and Kimoto 2012).

For xenobiology, functionally incorporating unnatural base pairs into organisms is a major goal of the field. In what the journal *Science* in 2014 listed as a runner-up for the ‘breakthrough of the year,’ the achievement ‘Giving life a bigger genetic alphabet,’<sup>197</sup> by Romesberg’s team. They accomplished the deployment of an unnatural base pair (dNaM-d5SICS) in *E. coli*, leading to the creation of a ‘semi-synthetic organism’ (Malyshev et al., 2014); this required the insertion of a plasmid that contained the unnatural base pair, which was retained by cells with high fidelity of replication; nevertheless, cells lost the unnatural base pairs over time and faced a decrease in fitness (its health, or ability to survive). The importance of Romesberg’s lab discovery in 2014 did not go unnoticed. For instance, Jim Thomas of the civil society group ETC Group stated in an email for the New York Times<sup>198</sup>:

While synthetic biologists invent new ways to monkey with the fundamentals of life, governments haven’t even been able to cobble together the basics of oversight, assessment or regulation for this surging field.

Romesberg’s team improved the system in 2017, replacing the unnatural base pair with a similar version called dTPT3 that resulted in a healthier semi-synthetic *E. coli* that retained its plasmid longer (Y. Zhang, Lamb, et al., 2017). They also used the base pair dNaM–

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<sup>197</sup> See Sachdev, M. 2014. Breakthrough of the Year: The top 10 scientific achievements of 2014. Dec. 18, 2014. Retrieved from <http://www.sciencemag.org/news/2014/12/breakthrough-year-top-10-scientific-achievements-2014> [last visited June 20, 2018].

<sup>198</sup> See Pollack, A. 2014. Scientists Add Letters to DNA’s Alphabet, Raising Hope and Fear. The New York Times, May 7, 2014. Retrieved from <https://www.nytimes.com/2014/05/08/business/researchers-report-breakthrough-in-creating-artificial-genetic-code.html> [last visited June 19, 2018].



dTPT3 to introduce non-natural amino-acids (called PrK and pAzF) into a protein that glows green (Y. Zhang, Ptacin, et al., 2017). This is aligned with the plans of Floyd Romesberg of using unnatural base pairs for producing proteins with non-natural amino-acids, for varying therapeutic purposes (i.e. development of new drugs based on proteins).

A different approach for incorporating unnatural base pairs in an organism was a top-down approach used by Phillipe Marlière and colleagues (2011). They replaced the majority of Thymine nucleotides in the genome of *E. coli* with the 5-chlorouracil analogue of Thymine. They added the 5-chlorouracil analogue to the growth medium of *E. coli* and favoured the use of this analogue by adaptive evolution, as cells were impaired from producing thymine naturally. This represents the first ‘semi-synthetic organism with an altered genetic alphabet’, suggesting that XNA-based life is possible. Similar chemical evolution experiments that changed the use of amino-acids by *E. coli* have been reported. For example, the growth of *E. coli* in the absence of Tryptophan, relying on the synthetic non-canonical amino acid thienopyrrole-alanine (Hoesl et al., 2015). In the second Xenobiology conference, Tobias Baumann presented his research on chemical evolution of *E. coli* to survive on indole derivatives instead of the amino acid Tryptophan (cf. Baumann et al., 2018).

Up to this point I have referred to efforts to develop unnatural base pairs that expand the repertoire of DNA. A further branch of the study of unnatural nucleic acids and alternative genetic systems concerns the modification of the tripartite chemical structure of nucleic acids, to include the backbone (sugar moieties and/or the phosphodiester backbone linkages), which sets them apart from the modification of nucleobases). The study of the properties of different XNAs partly has been motivated by the understanding of the origin and evolution of nucleotides that sustain life (cf. Eschenmoser 1999). As already explained, this class of unnatural nucleic acids have been called XNAs (for xeno-nucleic acids) (Herdewijn & Marlière, 2009). John Chaput’s lab in the University of California in Irvine provides an illustrative case of a research agenda on XNAs, that reflects a set of questions of interest for chemistry and biology that may pose useful applications for biotechnology. His website lists,

Collectively referred to as xeno-nucleic acids, or XNAs, these genetic polymers have unique physicochemical properties that include resistance to nuclease digestion and expanded chemical functionality. We envision a future where many of the same synthetic biology tools available to manipulate DNA and RNA are available to manipulate XNA. Such efforts open the door to a vast new world of synthetic genetics, where artificial genetic polymers can be used to create new tools for biotechnology and medicine, and possibly even improve our understanding of the origin of life itself.<sup>199</sup>

In terms of challenges to overcome, Chaput’s website shows

- Establishing new chemical synthesis strategies that produce XNA monomers on the gram to multi-gram scale and expand the chemical functionality of XNA beyond the natural bases of adenine (A), cytosine (C), thymine (T), and guanine (G).

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<sup>199</sup> From <https://chaputlab.com/research/> [last visited June 18, 2018].

- Designing new molecular evolution approaches that facilitate the production of XNA enzymes that can recognize and modify XNA substrates with high catalytic efficiency.
- Developing automated approaches that enable the rapid discovery of XNA aptamers and XNA catalysts to a broad range of biologically important targets.
- Elucidating the molecular structures of XNA enzymes and in vitro selected XNA aptamers and XNA catalysts to high resolution.

XNAs presents a different set of challenges to those faced with DNA, since methods for producing the modified nucleic acids need to be developed; DNA polymerases do not necessarily work in these cases and must be transformed to work with these chemicals. Hence, selection systems for new polymerases have been a limiting factor for the advancement of this field (Pinheiro & Holliger, 2012). Examples of alternative nucleic acids (XNAs) include TNA (L-alpha-threofuranosyl), which has a backbone structure composed of repeating threose sugars linked together by phosphodiester bonds (Ichida et al., 2005; Schoning et al., 2000). TNA nucleic acids have been suggested as a possible pathway to the formation of RNA molecules (Yu, Zhang, & Chaput, 2012), are resistant to nuclease degradation and can form base pairs complementary to strands of DNA and RNA. LNA (locked nucleic acids) are modified RNA nucleotides (ribofuranose), which have remarkable thermal and biological stability (Singh et al., 1998); they have been suggested as potential therapeutics for disease targets that are difficult to reach with current medicines, like Chronic hepatitis B (Gronweller & Hartmann, 2007; Javanbakht et al., 2018). Other ribofuranoses of interest are HNA (hexitol nucleic acids), in which like TNA, the natural ribose sugar found in RNA has been replaced with a nonribose sugar moiety (Verheggen et al., 1993). It has been reported to have functional properties for synthetic genetics, such as supporting heredity and evolution (Pinheiro et al., 2012). Another XNA category of nucleic acids is constituted by CeNA (cyclo- hexenyl nucleic acids) (Herdewijn & De Clercq, 2001) which also has useful properties for synthetic genetics (Pinheiro & Holliger, 2014). Deoxyxylonucleic acid (dXNA) has been reported as orthogonal nucleic acid candidate (Maiti et al., 2012). Furthermore, a more chemically distant range of nucleic acids include the use of acyclic moieties to link phosphate to base, such as GNA (glycerol nucleic acids) (Schlegel et al., 2007) and FNA (flexible nucleic acids) (Joyce et al., 1987). Peptide nucleic acids are a modification of backbone chemistry in which nucleobases are displayed on an aminoethylglycine back-bone, they display base-pairing with DNA and RNA, and are charge neutral (Nielsen et al., 1991); they are of interest in biotechnology for diagnostic assays and antisense therapies (Nielsen, 2010).

As xenobiology studies the possibilities of life outside biological constraints, it is hardly useful to box it into a series of themes. In a way, much of xenobiology stands for has been defined through the topics of the studies presented in the two xenobiology conferences held

so far in Genoa in 2014 and Berlin in 2016.<sup>200</sup> Besides the main theme of developing synthetic genetic chemistries (i.e., unnatural base pairs), next I will introduce seminal studies in expanding or recoding the genetic code, and the synthesis of proteins with amino-acids no existent in nature. Expanding the genetic consists of artificially modifying the genetic code, so that one or more specific codons are re-allocated to encode an amino acid that is not among the 20 common naturally-encoded proteinogenic amino acids; in other words, such expansion can be used to incorporate novel amino-acids into proteins (Chin, 2014; Xie & Schultz, 2005). Incorporating novel codons into proteins serves a variety of purposes, such as transforming proteins that enable their study (i.e., probing protein structure and function, post-translational modifications, regulation of protein activity, mode of action) or proteins with novel biological activities (such as more efficient enzymes, therapeutics, proteins that attach metals, or present less immunogenicity) that otherwise could not be achieved (Wang et al., 2009). For this end, orthogonal ribosomes that can process information in parallel and independently of wild type ribosomes have been reported (Rackham & Chin, 2005), as well as use ribosomes that operate a four-nucleotide codon system (Neumann et al., 2010). Further avenues include codon reassignment, such as repurposing of the amber codon (that codes for stopping translation) to code for a different amino-acid (Wang et al., 2001), or rare sense codon reassignment (codons that are rarely used in *E. coli* and expressed inefficiently) (Zeng, Wang, & Liu, 2014). Michael Jewett's lab has repurposed ribosomes, by tethering together different subunits of ribosomes (termed Ribo-T) that can incorporate unnatural amino acids or other compounds into protein synthesis, effectively constituting orthogonal genetic systems that could be evolved for novel functions without interfering with native translation (Orelle et al., 2015). The development of an orthogonal DNA replication (OrthoRep) system in yeast offers a platform independent of the cell. This synthetic replication system can reach high mutation rates, which can have applications for directed evolution of proteins (Ravikumar, Arrieta, & Liu, 2014).

The approaches for genetic code engineering explained above are capable of using only one non-standard amino acid at the time. For using multiple codons, one possibility is rewriting genome synthetically, the approach used by Craig Venter's team that led to the synthesis of an entire genome, producing the designed and partially synthetic species *Mycoplasma laboratorium* (Daniel G. Gibson et al., 2010). Such breakthrough prompted—at the time—U.S. President Barack Obama to request to the *Presidential Commission for the Study*

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<sup>200</sup> See footnote 14.

of *Bioethical Issues* (2010) to review the ethics and risks of synthetic biology,<sup>201</sup> which resulted in the report *New Directions: The Ethics of Synthetic Biology and Emerging Technologies*.

Laudable efforts in genome engineering or recoding have been reported by the lab of George Church, and his former post-doc Farren Isaacs (who attended the 2<sup>nd</sup> xenobiology conference). In 2011 they were able to replace all the TAG stop codon signals in the genome of *E. coli* for TAA, leaving TAG sequences free for encoding a new amino-acid; they called the highly efficient process ‘conjugative assembly genome engineering’ (CAGE) (Isaacs et al., 2011). This study probed the possibility of making genome-wide codon changes. Likewise, later on Church’s team reported the removal of one stop codon (TAG) from a bacterial genome, followed by the successful reassignment of its function, to a sense codon (a synonymous UAA stop codon, that could incorporate an amino acid of choice) that lacks the gene *release factor 1*, which terminates translation at UAG sites (Lajoie, Rovner, et al., 2013). They referred to this as the creation of a *Genomically Recoded Organism*. In the similar year they reported the removal of 13 (rare) codons of 42 genes, suggesting that genome-wide removal of various codons is feasible (Lajoie, Kosuri, et al., 2013). This was accomplished in 2016, what the authors call ‘rewiring.’ Church’s lab replaced 7 of the 64 genetic codons of *E. coli*, with others that encode the same amino-acids, showing the malleability of the genetic code (Ostrov et al., 2016) –but they yet had to reassemble those pieces into a functioning *E. coli*-. A similar effort of genome engineering, by Craig Venter’s team, created a synthetic cell that contains the smallest genome of any known, independent organism, functioning with just 473 genes essential for survival, that became known as JCVI-syn3.0 (Hutchison III et al., 2016); this is part of Craig Venter’s interest in establishing the minimal conditions for life.

Building on the previous work by Mark Lajoie and colleagues that reprogrammed genetic code of *E. coli* (Lajoie, Rovner, et al., 2013), Rovner et al., 2015 and Mandell et al., 2015<sup>202</sup> reported the dependency of recoded *E. coli* on unnatural amino acids, providing a form of auxotrophy (the nutritional requirement of a compound the organism cannot produce by itself) and hence a form of biological containment (more below on biocontainment and safety). By inserting specific aminoacyl-tRNA synthetase (aaRS)-tRNA pairs into the recoded *E. coli* strain, the authors were able to genetically reassign the UAG codon to encode for amino-acids that do not occur in nature and had to be fed to the cells. Next, they mutated essential proteins that incorporate these amino acids, so if the amino acids were not supplied in the growth media, they could not fabricate these proteins and would not survive. Mandell

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<sup>201</sup> See <https://bioethicsarchive.georgetown.edu/pcsbi/synthetic-biology-report.html> [last visited 19 June 2018].

<sup>202</sup> Note that both articles amend in their corrigendum their competing financial interests, as both studies have filed provisional applications with the US Patent and Trademark Office, to the names of George Church, Farren Isaacs and Alexis J. Rovner. The former two as founders of Enevolv Inc.

and colleagues (2015) accomplished this by engineering the *E. coli* strain so that engineered this strain so that UAG recodes for L-4,4'-biphenylalanine (bipA), and in the case of Rovner and colleagues (2015), they followed a similar approach with three different amino-acids: p-acetyl-L-phenylalanine (pAcF); p-iodo-L-phenylalanine (pIF) and or p-azido-L-phenylalanine (pAzF). What is remarkable about these two studies is that they were oriented towards achieving biocontainment, as they evaluated the escape frequencies of their mutated strains (that is, their ability to grow in the absence of the artificial amino acid), indicated by the growth (or lack of) of bacteria following days with a growth media that non-natural synthetic amino acids.

I have emphasized the research agenda of George Church and Farren Isaac, because they place particular attention to biocontainment (see also Gallagher et al., 2015), which as I will address in **chapters six** and **seven**, are a form of *built-in governance*, that favours a handling of risk that can be managed in the laboratory, and the continuation of a vision of governance established in the second Asilomar conference of 1975 (cf. Berg et al., 1975). For instance, for a news report for Nature by Elie Dolgin (2015) about both studies of Rovner and colleagues (2015) and Mandell and colleagues (2015), Farren Isaacs commented: “Establishing safety and security from the get-go will really enable broad and open use of engineered organisms.” Moreover, reflecting an imaginary of control that I propose in this dissertation, Dan Mandell commented “Our strains, to the extent that we can test them, won’t escape.” (Emphasis added). Noteworthy, these studies make the case for protection of bacterial strains from viruses, a problem that occurs in industrial biotechnology settings.

## Possibilities of xenobiology

This section offers an overview of potential applications and discoveries in xenobiology, that range from the development of novel therapeutics to understanding the origin of life on Earth. Phillipe Marlière promotes xenobiology with hype, in optimistic terms. While referring to the seminal publication of Romesberg lab (Malyshev et al., 2014), he commented:

It is easy to foresee that the enzymes will soon be enriched by a plethora of artificial links. In the next ten to fifteen years, *we can expect to see the emergence of biotechnology in a cornucopia of new products, ranging from pharmacy to textiles and electronics.* (Emphasis added).

Noteworthy, Marlière also established the connection between Xenobiology and commercial endeavours:

The same day that the work on the propagation of the XY pair in a cell was published, Floyd Romesberg announced the creation of his start-up Synthorx to exploit the invention in the field of health. The researchers have as objective the combination of 150 new amino acids in the therapeutic proteins.

Proteins with novel features can be used in a variety of settings, such as medicine, or industrial biotechnology. This is better explained by interviewee 14A, who comments that “what is required is that we have to show that the unnatural base pair can actually do something. Right now, it doesn’t do anything. It’s just being replicated inside of the cell. The ultimate goal is to have it used to encode proteins to actually encode the incorporation of unnatural amino-acids; there’s already ways of doing that.” I start this section by illustrating the case of Synthorx, as an example of what a viable technology derived from xenobiology approaches could look like. Founded by Floyd Romesberg, the start-up Synthorx<sup>203</sup> is one of a handful of start-ups actively pursuing xenobiology (although the company does not mention this field in its website). Its core business is the development of proteins that can incorporate non-natural amino-acids, which sets it closer to the field of protein engineering, than xenobiology.

The start-up Synthorx has developed a discourse that can be seen as removed from the type of biological questions that excite scientists to conduct research in xenobiology, to resemble a standardized, reliable platform for producing novel proteins. In the website of Synthorx, this is stated as:

The Synthorx platform provides an exclusive opportunity to incorporate multiple non-natural amino acids into large proteins at scale. Our platform operates outside of the natural coding framework of the organism, so it is not necessary to alter the coding structure of the host organism’s genome or re-appropriate existing codons. This orthogonal code provides access to significantly more genetic information storage capacity, which allows incorporation of multiple different non-natural amino acids encoded via many new codons without massive genome rewriting and interference between the natural and Synthorx systems.

The project of xenobiology is turned into providing ‘an exclusive opportunity to incorporate multiple non-natural amino acids into large proteins.’ This leaves a question unasked, about the usefulness of proteins that incorporate non-natural amino-acids. In the website of Synthorx it is also listed a table of applications is shown, which relate to tools of molecular biology, drug discovery, and related pharmaceuticals, like vaccines (**Figure 13**). Synthorx is a start-up with potential products in the pipeline, hence expectations of providing returns to investors. As such, it will be one of the channels through which the potential of xenobiology will be realized, or its applications reach the market.

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<sup>203</sup> See <http://synthorx.com/applications/> [Last visited March 31, 2017].

## Two new DNA bases, numerous solutions

With Synthorx's synthetic biology technology, we have many opportunities to create innovative new products for medical and life science applications.

Synthetic Base Pair	Expanded Genetic Alphabet	More Diverse Proteins
High Fidelity Replication	<i>In Vivo</i> Transcription	<i>In Vivo</i> Translation
Antisense, Aptamers, Beacons, Conjugation, DNA/RNA Sequencing, Gene Therapy, Nanomaterials, Oligos, Pathogen Diagnostics, Stapled DNA, SELEX, Vaccines	Aptamers, Conjugation, Diversity, Gene-expression Studies, Evolution, Labeling, Micro-RNA, RNA Trafficking, RNAi, Stapled RNA, Substitution	Antibody Drug Conjugates (ADC), Antimicrobials, Assays, Bi-cyclics, Biomarkers, BITE, Conjugation, Evolution, Libraries, Macrocycles, Specificity, Stapled Peptides, Protein Evolution, "Undruggable" Targets, Unnatural Amino Acids

Figure 13. Synthorx list of 'innovative new products.' Source: <http://synthorx.com/applications/>

Most likely the core applications that will derive of xenobiology are biomedical. A lab member commented that "I still see aptamers, sort of therapeutics, diagnostics, as the thing that is going to come out the quickest out of XNA."<sup>204</sup> If xenobiology delivers its promise of medical applications, like aptamers that can function as drugs, proteins with non-natural amino-acids that can serve as therapeutics, or providing useful diagnostic tools<sup>205</sup>, this sets a different tone for debates in the field. Is it necessary to redefine and transform the genetic machinery of life to produce novel drugs? If so, are the drugs or therapeutics that results from xenobiology, better than alternatives that are being developed by other means in the life sciences?

We should be cautious about justifying research in xenobiology as being a source of novel drugs. Questions about the biomedical industry are tied to questions of distribution, intellectual property, access to medication, experimentation in clinical trials, safety issues, and other issues. Just because a drug is created it does not mean that everyone will have access to it, and it needs to consider how existing health systems and health infrastructure must accommodate to incorporate novel ways of treating diseases. Access to medicines has become a global problem, giving rise to disputes over intellectual property in countries of the Global South, for example in the case of Novartis' drug *Imatinib* (cf. Rajan, 2015). Biomedical applications raise questions about the type of business models that xenobiology may enable, in the form novel forms of commercialization of products in the life sciences, or new business models.

<sup>204</sup> Aptamers are molecules (either DNA, RNA, proteins, or else) short in size which bind with very high affinity a specific 'target', often a protein. One of the problems associated with aptamers is that they are easily degraded inside the body, so aptamers made of XNA would be longer lasting inside the body and have a more effective therapeutic effect. For an overview of aptamers, see Keefe et al., 2010; and <https://www.basepairbio.com/research-and-publications/what-is-an-aptamer-2/> [last visited March 31, 2017].

<sup>205</sup> For example, the synthetic genetic system used in the Bayer *VERSANT* branched DNA diagnostic assay, used to diagnose patients with Hepatitis and HIV (Benner & Sismour, 2005).

Xenobiology also offers opportunities for different forms of distributing pharmaceuticals in the human body. Among these is the supply of pharmaceuticals in the human gut, via genetically modified bacteria.<sup>206</sup> Synthetic biologist 12A explains, in the context of orthogonal biology,

You can imagine scenarios where you can then put this *E. coli* in someone's gut to make it to an operation and you just make sure that this person takes [a] pill every day that keep this compound there, [to keep the *E. coli* alive], but then when you want the *E. coli* to die away, or you don't want any in the sewer system, it's just a matter of the person stops taking the drug.

These visions of control of microorganisms, such as generating a new form of supplying pharmaceuticals to the human body, have the potential to reconfigure the relationship with our bodies, our health, and our medicines. Needless to say, it is materially different ingesting a pill as from maintaining a 'living factory' of a pharmaceutical in your body, establishing a different relationship, a form of symbiosis, between microorganisms and humans.

An entirely different set of applications for xenobiology stem from the perennial question of the '*origin of life*', or how living organisms came into existence<sup>207</sup>. Interest in the field has attracted researchers like Steven Benner, and Phil Holliger, who have claimed that knowledge about the biophysics and chemistry of DNA, and the mechanisms behind DNA replication, can provide important clues for understanding life. Xenobiology can contribute to the question of whether life on Earth could have evolved to be based on a chemistry different to that of DNA. Benner et al. (2003: 125) write:

The elegance of the structure of terreal DNA prompts the general question: Is its structure universal? If life arose in the cosmos independently of life on Earth, would it use exactly the same genetic material? *Or can alternative chemical structures support rule-based molecular recognition as well?* (Emphasis added).

In a similar vein, –in the video made by Biofaction of the first xenobiology conference,<sup>208</sup> Phil Holliger addresses similar questions:

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<sup>206</sup> This possibility has been already explored by Steidler and colleagues (2003) (who develop a biocontainment system for release of the bacteria *Lactococcus lactis* in the human intestine), so it is not a unique possibility of xenobiology. In fact, this form of therapy, 'orally delivered biopharmaceuticals', is already being pursued. This allows the selective delivery of biological and small molecule pharmaceuticals to the oral and gastrointestinal tract, for cases when mechanisms like injectable medicines are not efficient. For instance, this has been pursued by the Belgian start-up Actinogenix, now purchased by Intrexon. The company initiated the research-product line *ActoBiotics*. See 'Intrexon Acquires ActoGenix for \$60M', *Genetic Engineering and Biotechnology News*, February 13, 2015. From <https://www.genengnews.com/gen-news-highlights/intrexon-acquires-actogenix-for-60m/81250929> [last visited January 15, 2018]; Actobiotics. Intrexon website. From <https://www.dna.com/Technologies/ActoBiotics> [last visited January 15, 2018]. For publications in the scientific literature on Actobiotics, see <https://www.dna.com/Technologies/Peer-Reviewed-Publications> [last visited January 15, 2018].

<sup>207</sup> See Malaterre (2009) for a philosophical inquiry on the possibility of synthetic biology to shed light on the origins of life and redefinitions of life. For an introduction on the topic of 'origin of life', see Maynard Smith & Szathmáry (2000).

<sup>208</sup> See footnote 14.



One of the key things that xenobiology will tell us about is *if the chemistry of life is in some way special*, functionally privileged, superior to other chemistries that we might think of. Or if really, if life sort of arose in an opportunistic way, making use of the building blocks that were available, and building on that. So I think that is a truly fundamental question in biology to understand that (Emphasis added).

As Holliger points out, this is a fundamental question for biology, in the form of counterfactual questions over the role of DNA in ‘life as we know it’. These questions sparked further research in the field. For instance, Benner (2004: 626), after referring to a paper that highlights the role of the mineral borate in the evolution of the nucleic acid RNA,<sup>209</sup> write that “[t]he structure of our DNA may therefore reflect the minerals that were present in ancient deserts on early Earth.” However, it is difficult for xenobiology to provide answers that go beyond supporting the idea that XNA polymers could indeed support biological evolution (i.e. Pinheiro et al., 2012); understanding why DNA resulted as the genetic molecule of life on Earth, is a question that is still being researched.

As Benner et al. (2003: 125) write, highlighting the role of imagination, “[to] answer these questions requires that *alternative structures be imagined*, and that the power of contemporary synthetic organic chemistry be applied to prepare them in the laboratory.” (Emphasis added). In practice, research in xenobiology may not be that different from organic chemistry, or molecular biology. But the guiding questions, and the definition of life that it entails, distinguish it from other disciplines, enabling exciting research to be conducted. As I argue in this dissertation, Xenobiology can be seen as a project of imagining a different biology, placed in a (virtual) biological world—as Marlière would put it—a world that could have existed, but did not. What we are witnessing nowadays is the unfolding of this imagination into material objects, made possible through the work in a laboratory using tools derived from molecular biology, plus the potent approach of directed evolution.

The reach of imagination is important when it comes to understanding how among the most precious goals of xenobiology is developing organisms that can function with XNA. But imagination also comes in the form of asking questions, of asking about the limits of the biologically possible. Interviewee 5C goes a step further, connecting questions over the uniqueness of DNA, with the possibility of having cells working with XNA. Referring to earlier work in DNA biochemistry and hydrogen bonding by Eric Kool at Stanford, comments:

The most basic question is –what is the requirement for information storage and retrieval?– ... “that was a very important, inspirational part for my work, and so we’ve been sort of extending that idea and saying –look, in terms of replication in a cell, transcription in a cell, and translation at a ribosome in a cell, what are the physical requirements?– can you just get any force that causes nucleotides to pair? or is there really something special to A, C, G and T, and that nature’s evolution selected for them?”

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<sup>209</sup> See Benner et al., 2004.

Research has shown that [t]he capacity of synthetic polymers for both heredity and evolution also shows that DNA and RNA are not functionally unique as genetic materials. (Pinheiro et al., 2012: 344). This seems to settle the question of whether life could have evolved based on a different genetic material. Nevertheless, in a conversation with a prominent chemist who conducts research in the origin of life, I commented to him that I was studying the social and political aspects of xenobiology and asked about the relevance of this field for studies in the origin of life. The chemist made clear that he did not consider advances in xenobiology to be relevant for the origin of life and established some distance from this field.

A dilemma that xenobiology faces consists of being in the middle of highly interesting questions for biology, such as –could life have been based on a different genetic system?– and providing interesting applications, like new pharmaceuticals, diagnostic tests, and biocontained organisms. It is this tension that I find interesting — how scientists navigate a knowledge production regime that demands that scientific research produce valuable outputs, while at the same time favours innovative, ground-breaking research that contributes to solving fundamental questions in science. Interviewee 8B summarizes this tension, by saying, “the origin of life is all very basic research, which is quite challenging, and because of that, the funding opportunities are limited. Xenobiology is also extremely challenging [to find funding for] but there are these, at least in the mid-term, very clear useful applications, so *it's more fundable*.” (Emphasis added).

In summary, xenobiology faces a tension between addressing highly interesting research questions and providing ground-breaking applications that fulfil the promise of a vibrant biotechnological industry. This begs to ask whether xenobiology will deliver its promises. Some of the scientists I interviewed were sceptical about the potential of xenobiology and were cautious about providing unsupported hype. For example, this is reflected in the passage,

We are still a long way from robust orthogonal systems that can be used for practical applications. System-specific replication machinery needs to be developed to truly insulate XNA from DNA-based life forms. Current working orthogonal systems are natural-xeno hybrids (Moe-Behrens et al., 2013: 6).

Furthermore, synthetic biologist 8B commented that

You only see a field take off when it is powerful and general enough that people can do tons of useful things with it. Whether that's new investigations into fundamental phenomenon, or new technologies or applications which have practical uses. And it *doesn't look like xenobiology is there yet*, but it's certainly moved a lot more in the, say, past five years, than the past ten or twenty (Emphasis added).

They claimed that the future of the field was unpredictable, and current research efforts could be commercialized ten years down the road, but the benefits could be immense. This reflects an acknowledgment of the technical difficulties to overcome. In order to survive as a

discipline and recruit funds and resources, xenobiologists must promote their field as a provider of solutions, although solutions may not be immediate. Scientists understand that the possibilities of xenobiology are dictated by biology; what is biologically doable determines what can be done with xenobiology. This is reflected in how interviewees referred to xenobiology in a humble way, recognizing the difficulty of modifying the foundations of biology. Interviewee 5C expressed that “what we do is really only the *first baby steps* into this whole idea of creating new forms of life.” (Emphasis added). In a similar vein, 8B commented:

We were hoping to do one millionth as well as nature starting out. And I think if we're getting closer and closer to what nature can achieve, that's a point in which we should start being concerned, in thinking about responsible ways of controlling it, but we're very far away from that point.

As scientists refer to their efforts with humility, being far from producing useful applications, and being incapable of determining what these might be, the field keeps moving forward, and a space must be created to ask the right questions as it progresses.

## Appendix 2. List of secondary sources

In this section I display a list of scientific articles that have received media coverage, along with a sample of news and media products, including interviews and panel discussions. This list provide examples of the type of secondary sources from news and media; the sources indicated in this section are representative of a body of sources about synthetic biology and xenobiology, not listed in their totality for reasons of space.

Date of publication	Scientific article	Media source	Website address	Title
July 14, 2011	Isaacs et al., 2011	National Geographic	<a href="https://www.nationalgeographic.com/science/phenomena/2011/07/14/hacking-the-genome-with-a-mage-and-a-cage/">https://www.nationalgeographic.com/science/phenomena/2011/07/14/hacking-the-genome-with-a-mage-and-a-cage/</a>	Hacking the genome with a MAGE and a CAGE
April 20, 2012	Pinheiro et al., 2012	National Geographic	<a href="https://news.nationalgeographic.com/news/2012/04/120419-xna-synthetic-dna-evolution-genetics-life-science/">https://news.nationalgeographic.com/news/2012/04/120419-xna-synthetic-dna-evolution-genetics-life-science/</a>	Synthetic DNA Created, Evolves on Its Own
April 19, 2012	Pinheiro et al., 2012	Scientific American	<a href="https://www.scientificamerican.com/article/enzymes-grow-artificial-dna/?redirect=1">https://www.scientificamerican.com/article/enzymes-grow-artificial-dna/?redirect=1</a>	Enzymes Grow Artificial DNA
April 19, 2012	Pinheiro et al., 2012	Discover Magazine	<a href="http://blogs.discovermagazine.com/notrocketscience/2012/04/19/synthetic-xna-molecules-can-evolve-and-store-genetic-information-just-like-dna/#.XPV0Ry2ZNbU">http://blogs.discovermagazine.com/notrocketscience/2012/04/19/synthetic-xna-molecules-can-evolve-and-store-genetic-information-just-like-dna/#.XPV0Ry2ZNbU</a>	Synthetic XNA molecules can evolve and store genetic information, just like DNA
January 21, 2015	Mandell et al., 2015	Harvard Medical School	<a href="https://hms.harvard.edu/news/no-escape">https://hms.harvard.edu/news/no-escape</a>	No Escape: Biological safety lock for genetically modified organisms
May 21, 2014	Malyshev et al., 2014	CBC Radio show The Current	<a href="http://www.cbc.ca/radio/thecurrent/may-21-2014-1.2908110/expanding-the-alphabet-of-life-with-artificial-dna-1.2908115">http://www.cbc.ca/radio/thecurrent/may-21-2014-1.2908110/expanding-the-alphabet-of-life-with-artificial-dna-1.2908115</a>	Expanding the alphabet of life with artificial DNA [interview to Floyd Romesberg (Scripps Research Institute) and Jim Thomas (ETC Group)]
May 7, 2014	Malyshev et al., 2014	The New York Times	<a href="https://www.nytimes.com/2014/05/08/business/researchers-report-breakthrough-in-creating-artificial-genetic-code.html">https://www.nytimes.com/2014/05/08/business/researchers-report-breakthrough-in-creating-artificial-genetic-code.html</a>	Scientists Add Letters to DNA's Alphabet, Raising Hope and Fear
May 7, 2014	Malyshev et al., 2014	Nature	<a href="http://www.nature.com/news/first-life-with-alien-dna-1.15179">http://www.nature.com/news/first-life-with-alien-dna-1.15179</a>	First life with 'alien' DNA
December 1, 2014	Taylor & Holliger, 2015	University of Cambridge	<a href="http://www.cam.ac.uk/research/news/worlds-first-artificial-enzymes-created-using-synthetic-biology">http://www.cam.ac.uk/research/news/worlds-first-artificial-enzymes-created-using-synthetic-biology</a>	World's first artificial enzymes created using synthetic biology
January 23, 2015	Mandell et al., 2015	Radio show Science Friday	<a href="https://www.sciencefriday.com/segments/scientists-engineer-bacteria-with-genetic-kill-switch/">https://www.sciencefriday.com/segments/scientists-engineer-bacteria-with-genetic-kill-switch/</a>	Scientists Engineer Bacteria With Genetic 'Kill Switch' [Interview with Dan Mandell (Harvard Medical School) and Dave Guston (Arizona State University)]
January 21, 2015	Mandell et al., 2015; Rovner et al., 2015	The Guardian	<a href="http://www.theguardian.com/science/2015/jan/21/genetically-recoded-organisms-artificial-compounds">http://www.theguardian.com/science/2015/jan/21/genetically-recoded-organisms-artificial-compounds</a>	Scientists create GM organisms reliant on artificial compounds for survival

<b>January 27, 2015</b>	Mandell et al., 2015; Rovner et al., 2015	The Washington Post	<a href="https://www.washingtonpost.com/news/energy-environment/wp/2015/01/27/scientists-are-actually-creating-microscopic-life-in-laboratories-should-you-worry/">https://www.washingtonpost.com/news/energy-environment/wp/2015/01/27/scientists-are-actually-creating-microscopic-life-in-laboratories-should-you-worry/</a>	Scientists are actually creating microscopic life in laboratories. Should you worry?
<b>November 16, 2015</b>	DiCarlo et al., 2015	Nature	<a href="https://www.nature.com/news/safety-upgrade-found-for-gene-editing-technique-1.18799">https://www.nature.com/news/safety-upgrade-found-for-gene-editing-technique-1.18799</a>	Safety upgrade found for gene-editing technique
<b>January 18, 2016</b>	Tack et al., 2016	New Scientist	<a href="https://www.newscientist.com/article/2073570-gene-change-could-stop-gm-bacteria-surviving-outside-the-lab/">https://www.newscientist.com/article/2073570-gene-change-could-stop-gm-bacteria-surviving-outside-the-lab/</a>	Gene change could stop GM bacteria surviving outside the lab
<b>August 18, 2016</b>	Ostrov et al., 2016	Science	<a href="https://www.sciencemag.org/news/2016/08/biologists-are-close-reinventing-genetic-code-life">https://www.sciencemag.org/news/2016/08/biologists-are-close-reinventing-genetic-code-life</a>	Biologists are close to reinventing the genetic code of life
<b>January 24, 2017</b>	Zhang et al., 2017	The Guardian	The Guardian Organisms created with synthetic DNA pave way for entirely new life forms	<a href="https://www.theguardian.com/science/2017/jan/23/organisms-created-with-synthetic-dna-pave-way-for-new-entirely-new-life-forms">https://www.theguardian.com/science/2017/jan/23/organisms-created-with-synthetic-dna-pave-way-for-new-entirely-new-life-forms</a>

Table 2. List of news articles and interviews about recent scientific articles in xenobiology.

<b>Date of publication</b>	<b>Media source</b>	<b>Website address</b>	<b>Title of article</b>
<b>September 11, 2014</b>	<i>ABC Blogs</i>	<a href="http://abcblogs.abc.es/bacterias-batallas/2014/09/11/biologia-sintetica-victor-lorenzo">http://abcblogs.abc.es/bacterias-batallas/2014/09/11/biologia-sintetica-victor-lorenzo</a>	Victor de Lorenzo: «Los genes y el metabolismo son como los políticos y la economía»
<b>August 3, 2016</b>	<i>Nature</i>	<a href="https://www.nature.com/naturejobs/science/articles/10.1038/nj7614-117a">https://www.nature.com/naturejobs/science/articles/10.1038/nj7614-117a</a>	Turning point: Kevin Esvelt
<b>July 1, 2014</b>	<i>Scoop</i>	<a href="http://www.suzanmazur.com/?p=259">http://www.suzanmazur.com/?p=259</a>	An interview with Jack Szostak
<b>May 11, 2016</b>	<i>The Harvard Gazette</i>	<a href="https://news.harvard.edu/gazette/story/2016/05/if-youre-not-failing-youre-probably-not-trying-as-hard-as-you-could-be/">https://news.harvard.edu/gazette/story/2016/05/if-youre-not-failing-youre-probably-not-trying-as-hard-as-you-could-be/</a>	George Church's scientific drive
<b>May 25, 2009</b>	<i>UC Santa Cruz</i>	<a href="https://scicom.ucsc.edu/publications/QandA/2009/benner.html">https://scicom.ucsc.edu/publications/QandA/2009/benner.html</a>	Steve Benner, synthetic biologist
<b>June 8, 2016</b>	<i>BioEdge</i>	<a href="https://www.bioedge.org/bioethics/interview-with-nelson-l.-michael-presidential-commission-for-the-study-of-b/11910">https://www.bioedge.org/bioethics/interview-with-nelson-l.-michael-presidential-commission-for-the-study-of-b/11910</a>	Interview: "Democratic deliberation" and bioethics
<b>March 23, 2012</b>	<i>Live Science</i>	<a href="http://www.livescience.com/19264-understanding-synthetic-biology-boeke-nsfbts.html">http://www.livescience.com/19264-understanding-synthetic-biology-boeke-nsfbts.html</a>	Q&A: Demystifying Synthetic Biology
<b>October 13, 2013</b>	<i>The Guardian</i>	<a href="https://www.theguardian.com/science/2013/oct/13/craig-ventner-mars">https://www.theguardian.com/science/2013/oct/13/craig-ventner-mars</a>	Craig Venter: "This isn't a fantasy look at the future. We are doing the future"
<b>November 19, 2010</b>	<i>The Scientist</i>	<a href="https://www.the-scientist.com/daily-news/qa-ethics-chair-on-synthetic-biology-42964">https://www.the-scientist.com/daily-news/qa-ethics-chair-on-synthetic-biology-42964</a>	Q&A: Ethics chair on synthetic biology
<b>December 5, 2011</b>	<i>Chemistry Views</i>	<a href="https://www.chemistryviews.org/details/ezone/1376211/Interview_with_Frances_H_Arnold_Design_by_Evolution.html">https://www.chemistryviews.org/details/ezone/1376211/Interview_with_Frances_H_Arnold_Design_by_Evolution.html</a>	Interview with Frances H. Arnold – Design by Evolution
<b>November 4, 2012</b>	<i>Science 2.0</i>	<a href="https://www.science20.com/randall_mayes/discussion_george_church_about_his_new_book_regenesis_and_synthetic_biology-95999">https://www.science20.com/randall_mayes/discussion_george_church_about_his_new_book_regenesis_and_synthetic_biology-95999</a>	A Discussion with George Church On His New Book RegenesiS And Synthetic Biology

<b>May 8, 2015</b>	<i>National Non-Food Crops Centre (NNFCC)</i>	<a href="http://news.bio-based.eu/interview-dr-lionel-clarke-director-of-bionerg-and-co-chair-of-the-governments-synthetic-biology-leadership-council-sblc/">http://news.bio-based.eu/interview-dr-lionel-clarke-director-of-bionerg-and-co-chair-of-the-governments-synthetic-biology-leadership-council-sblc/</a>	Interview: Dr Lionel Clarke, Director of BionerG and Co-Chair of the Government's Synthetic Biology Leadership Council (SBLC)
<b>May 29, 2015</b>	<i>The Bioart Society</i>	<a href="https://www.biofaction.com/interview-oron-cattsmarkus-schmidt/">https://www.biofaction.com/interview-oron-cattsmarkus-schmidt/</a>	Interview Oron Catts/Markus Schmidt
<b>April 21, 2016</b>	EUSynbioS	<a href="http://www.eusynbios.org/blog/2016/4/21/taking-synbio-out-of-the-lab-an-interview-with-britt-wray">http://www.eusynbios.org/blog/2016/4/21/taking-synbio-out-of-the-lab-an-interview-with-britt-wray</a>	Taking synbio out of the lab: an interview with Britt Wray.
<b>August 26, 2014</b>	PLOS Blogs	<a href="https://blogs.plos.org/synbio/2014/08/26/synthetic-biology-gone-wild-probably-not-plos-synbio-interview-with-tom-ellis/">https://blogs.plos.org/synbio/2014/08/26/synthetic-biology-gone-wild-probably-not-plos-synbio-interview-with-tom-ellis/</a>	Synthetic Biology Gone Wild? Probably Not. An interview with Tom Ellis
<b>September 17, 2010</b>	Science	<a href="http://www.sciencemag.org/careers/2010/09/expanding-genetic-code">http://www.sciencemag.org/careers/2010/09/expanding-genetic-code</a>	Expanding the Genetic Code

Table 3. List of interviews with researchers about synthetic biology and xenobiology.

## Appendix 3. Consent to research form (For participant observation)

### CONSENT TO RESEARCH FORM

**Title of Project:** 'Imaginations and visions associated with the development of bottom-up synthetic biology'

**Researcher:** Mr. Alberto Aparicio

**Affiliation:** PhD student, Department of Science & Technology Studies, UCL

**Tick box if you agree**

1. I confirm that I have read and understood the information sheet dated 13-Jan-2016 for the above study and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and that I am free to withdraw at any time during the data collection phase, without giving any reason.
3. I agree that words that I use during the period of research can be used anonymously, in the presentation and publication of the research.
4. I agree to take part in the above study.

**For further details, please contact:** Mr. Alberto Aparicio, Department of Science & Technology Studies. University College London. 22 Gordon Square, London, WC1E 6BT.  
alberto.aparicio.13@ucl.ac.uk / Tel: +44 (0) 7549 [REDACTED]

#### Participant Information

Name \_\_\_\_\_

Address \_\_\_\_\_

Email \_\_\_\_\_

**Participant signature**

Signature \_\_\_\_\_

Date \_\_\_\_\_

**Researcher signature**

Signature \_\_\_\_\_

Date \_\_\_\_\_

*1 copy for participant, 1 copy for researcher*



## Appendix 4. Consent form for research interviews

### INFORMATION AND CONSENT FORM FOR DOCTORAL RESEARCH INTERVIEWS

#### Information on Doctoral Research for Interviewee

Working title of project: *'Imaginaries and visions associated with the development of bottom-up synthetic biology'*

Name of researcher: Alberto Aparicio

Researcher contact information: [alberto.aparicio.13@ucl.ac.uk](mailto:alberto.aparicio.13@ucl.ac.uk) / +44 (0)7549 [REDACTED]

Researcher affiliation:

PhD student

Department of Science and Technology Studies, University College London

22 Gordon Square, London, WC1E 6BT

This doctoral research projects aims to understand how the research agenda of synthetic biology and xenobiology is influenced by society and politics.

The data collected from interviews will be used for my research in the form of anonymous quotations and quantitative analyses involving word frequency and word association.

#### Consent to Doctoral Research from Interviewee

In consideration of the work that Alberto Aparicio is doing to collect and preserve impressions and perspectives regarding development of synthetic biology and its social, political and ethical associations, I give him consent to use the information from my recorded interview for his doctoral research, publications, and presentations on these subjects.

1. I understand that I have the option to withdraw my contribution to this research at any time and without giving reason, before and during the interview. After the interview is conducted, I may withdraw my participation during the next four weeks, by contacting Alberto Aparicio via email at [alberto.aparicio.13@ucl.ac.uk](mailto:alberto.aparicio.13@ucl.ac.uk).

2. I understand that the information from my interview may be recorded, with my permission. Alberto Aparicio will make all possible efforts to ensure that it will not be possible to identify me in the research published or presented. Information in the interview will be made anonymous, in order to protect my identity. In the case that Alberto Aparicio decides to transcribe my recorded interview for an archive, he will send the transcript to me via email. From the date I receive the transcript, I will have two weeks to indicate whether its content should not be used. If I do not state that the transcript cannot be used, Alberto Aparicio will consider the transcript has been approved.
  
3. I understand that my recorded interview will be protected and held by Alberto Aparicio for five years following doctoral research completion. All recordings, transcripts, and notes will be securely disposed five years following doctoral research completion.
  
4. I understand that I have copyright to my recorded interview. I consent to transfer copyright to Alberto Aparicio for his research objectives and this will result in a joint-ownership of the recorded interview.

I understand that Alberto Aparicio has completed the required 'Ethics Procedures' and has been approved by the Ethics Committee through the Department of Science and Technology Studies at University College London. **The application reference number (Ethics reference) for this study is 2015-12-01.**

I understand that my signature below provides consent for the information above.

**PROCESSING NUMBER**

**INTERVIEWEE INFORMATION**

Name \_\_\_\_\_

Address \_\_\_\_\_

Email \_\_\_\_\_

**INTERVIEWEE SIGNATURE**

Signature \_\_\_\_\_

Date \_\_\_\_\_

**INTERVIEWER SIGNATURE**

Signature \_\_\_\_\_

Date \_\_\_\_\_

*1 copy for participant, 1 copy for researcher*

## Appendix 5. Participant information sheet

### PARTICIPANT INFORMATION SHEET

**Title of project:** 'Imaginations and visions associated with the development of bottom-up synthetic biology'

UCL Department of Science and Technology Studies application reference number 2016-01-13

If you need help reading this sheet, please ask for help from anyone you would like

*I am asking you to take part in a research study. I want you to understand why I am doing the study and what it will involve. Then you will be able to make a decision about taking part. Please read this sheet carefully. Discuss it with other people if you want. Feel free to ask me for more information or to explain something you do not understand.*

*Ask me if there is anything that is not clear or if you would like more information about.*

#### **1. What is the purpose of this research study?**

The purpose of this study is to learn more about the influence of social, ethical and political factors in research conducted at the laboratory level, in the field of synthetic biology.

In addition, this study will explore novel forms of collaboration between social and natural scientists.

#### **2. Why were you chosen?**

You have been approached to participate in this study because you work or conduct research in a synthetic biology laboratory.

#### **3. Do you have to take part?**

It is up to you to decide whether or not to take part. If you decide to take part then I will ask you to sign a Consent Form. Note that you may decide to take part, not to take part, or pull out once you have started. If you choose to pull out, you do not have to give a reason, but withdrawal would not be possible while I am analysing and writing the PhD thesis; this process is expected to start in spring 2017. None of these decisions will affect you or your university in any way.

#### **4. What will happen to you if you take part?**

If you volunteer to take part, you will be involved in a piece of 'participant observation' (or 'ethnography'). This means that I will visit your laboratory for about eighteen months, time in which I may observe you at your workplace and have occasional conversations with you.

At a later stage, I may organize workshops and roundtable discussions with members of your laboratory.

#### **5. How is data going to be used?**

I may want to quote you in my PhD thesis. All quotations would be anonymous – you would not be named or identified.

#### **6. What do you have to do?**

There are no special restrictions or requirements if you take part.

#### **7. What are the possible disadvantages or risks of taking part?**

I do not expect there will be any disadvantages. If you consider there would be disadvantages if you participate in this study, please let me know.

There is subtle risk that your identity may be identified in the published material of this study. Note that all participants will be anonymised and I will adopt full measures to protect your identity and ensure your anonymity. In addition, the content of your research activities will be kept confidential as much as possible.

#### **8. What are the possible benefits of taking part?**

There are no monetary benefits for taking part in this research. I hope that my involvement in your laboratory provides new perspectives about your work, especially in terms of how it is related to society and science policy.

#### **9. What happens when the research study stops?**

You will continue with your work and activities as usual. Nothing will be changed by taking part in this study.

#### **10. What if something goes wrong?**

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed.

**11. Will your participation in this study be kept confidential?**

Yes. All the information about your participation in this study will be kept confidential. The data that I collect from you would not be passed onto your workplace or any other authority.

All the data will be stored in locked cabinets at University College London according to the Data Protection Act 1998. Any information about you that leaves the department will have your name and any identifying features removed so that you cannot be recognised from it.

**12. What will happen if you do not want to carry on with the study?**

You are able to withdraw from the study at any time without having to give a reason.

**13. What if there is a problem?**

**Complaints:**

If you have a concern about any aspect of this study, you should ask to speak with me and I will do my best to answer your questions (My mobile No. is (0)7549 645890); alternatively, you can communicate your concerns to your laboratory principal investigator. If you remain unhappy, please contact the *postgraduate research programme tutor* of the Science and Technology Studies Department of University College London at [sts-pgtutor@ucl.ac.uk](mailto:sts-pgtutor@ucl.ac.uk), [mentioning the application reference number 2016-01-13](#)

**Harm:**

This research will be indemnified under the University's legal liability insurances. In the event that something does go wrong, and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against University College London but you may have to pay your legal costs.

**14. What will happen to the results of the study?**

I expect to use the results of the study in my PhD thesis. I will also present my results at academic meetings, may publish my findings in journals or academic books. You will never be personally identified.

**15. Who is organising and funding the research?**

This research project does not have any external funding. PhD studies of Alberto Aparicio are funded by Colciencias, a government agency that funds science and technology research in Colombia.

This research is organised by the Department of Science & Technology Studies at University College London, as a component of my PhD programme.

**17. Contact for further information**

Mr. Alberto Aparicio

Department of Science & Technology Studies

University College London

22 Gordon Square, London, WC1E 6BT

Tel: +44 (0) 7549 [REDACTED]

If you take part you will be given a copy of this information sheet and your signed consent form to keep.

**THANK YOU FOR TAKING PART IN THIS RESEARCH**