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Life as Engineerable Material: An ethnographic study of synthetic biology

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Declaration

I certify that the thesis I have presented for examination for the MPhil/PhD degree of the London School of Economics and Political Science is solely my own work other than where I have clearly indicated that it is the work of others (in which case the extent of any work carried out jointly by me and any other person is clearly identified in it).

I warrant that this authorisation does not, to the best of my belief, infringe the rights of any third party.

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Abstract

Synthetic biology is an emerging hybrid discipline that aims to apply an engineering approach to biology, in order to render biology controllable, predictable, and ultimately engineerable. Herein I explore synthetic biology as a project to control life at the molecular level through the lens of an ethnographic study of a newly formed academic synthetic biology research centre.

Within this overarching narrative, I tease out two main stories regarding the field. First, I explore the topic of disciplinarity, investigating the work being done to establish synthetic biology as a hybrid discipline. Drawing on the ideas of repertoire, doability, and epistemic cultures, I explore the conflicts and compromises inherent in the attempt to form a hybrid discipline out of biology and engineering. I describe the strategies being employed to bridge this epistemic cultural divide, and the challenges in doing so.

Second, I explore the work being done to bring the goals of the discipline to fruition. Synthetic biology's dream of rendering biology engineerable is rooted in a reductionistic vision of life. This approach to biology raises both practical and conceptual issues. Thus, in exploring this story I address both the practical day-to-day work of synthetic biologists attempting to apply an engineering approach to biology, and the challenges these synthetic biologists face in conceptualising the products of that work.

Third, I draw these stories together and show that synthetic biology is one among many disciplines emerging at the intersection of biology and engineering. I suggest that this fertile, if complicated, disciplinary crossroads may be the site of a conceptual shift in the way we 'do' and think about biology and ultimately, life.

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Chapter One: Introduction

> *I suppose some time in 2005 . . . I started to think . . . systems biology is about analysing biological systems, I thought, I'm an engineer, I mean this sounds like . . . you should be able to . . . make stuff, synthesise it, you know, out of all this, because . . . the cell is the ultimate manufacturing unit, that's the term I used . . . which I think is quite catchy. OK, so I thought . . . cells should be able to manufacture stuff . . . if you can modify DNA, which is essentially the code, you should be able to put this into a cell and it should be able to produce something, you see. I got quite excited about this . . . and I went to do one of my regular visits to . . . MIT, and . . . I . . . walked over to the civil engineering department, walked into this office, and there was Drew Endy and Randy Rettberg! . . . and I told them my ideas and I said, 'What do you think about this, do you think it's crazy?' and they said, 'No it's not at all crazy but it's called synthetic biology.'*
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> (Alan, senior researcher, engineering)[1]

Some may contend that this does indeed sound crazy, or perhaps that using biological cells as manufacturing units to produce desired products is the stuff of science fiction, not reality. However, to a growing, and international, group

[1] In order to provide some biographical information for my research participants, while also maintaining their anonymity, each participant is referred to by a pseudonym as well as their broad role within the academic research centre (doctoral student, postdoctoral researcher or senior researcher) and the 'side' they come from, either biology or engineering. However, given that the research centre is such a prominent site within the UK and European synthetic biology community, it is difficult to maintain its anonymity. Likewise, despite my efforts, it is incredibly difficult to guarantee the confidentiality and anonymity of my research participants, especially those in prominent positions. This has been an issue both for the writing of this thesis, and for the writing of conference papers and academic publications. I have anonymised my participants, and the Centre, as much as possible when writing or speaking about them, but it is possibly that someone with intimate knowledge of the Centre, or of the UK synthetic biology community, could be able to identify them. This is something I have discussed on several occasions with the members of the Centre, and is something that continues to concern me.

of scientists and engineers like Alan, this is an exciting new frontier. Alan Gregg, an electrical engineer by training, is one of two directors of the biggest, most prominent and well-funded synthetic biology research centre in the United Kingdom, a centre which was to become my fieldwork site, and which will, from here on be referred to as 'the Centre.' Alan's origin story for the Centre started back in 2005 when he first got the idea, as he describes above, of applying his engineering know-how to biology in order to "*manufacture stuff*." On Alan's return from the Massachusetts Institute of Technology (MIT) to the UK he contacted biochemist Malcolm Brown, who he referred to during my interview with him as his "*pet biologist,*" and told him about this new 'synthetic biology.' Like Alan, Malcolm embraced the idea of engineering biology with enthusiasm, and that, Alan claims, is how synthetic biology got underway at the prestigious university where they work.

In 2006 they entered their first team in the international genetically engineered machines competition, or iGEM. A challenge for teams of undergraduate students to design and construct synthetic biology 'products' over the summer and then compete against each other at MIT in November.[2] This was only the second year that teams from outside the US were involved in iGEM and Alan and Malcolm's team came second, a fact they repeat often, and with great pride. Following this success, and with Alan's enthusiasm and conviction that synthetic biology was primed to be the next 'big thing,' Alan and Malcolm successfully appealed to the university rector for the funding to set up a small synthetic biology laboratory. This endowment was followed, in 2009, by a large amount of research council funding from the EPSRC[3] in the form of a science and innovation award. Alan and Malcolm used this money to set up, and staff, a much larger research centre, which opened its doors in April 2010.

Thus, in December 2009 when I started my fieldwork, the Centre was still getting up and running. Many of the staff were new, the laboratories were

[2] For a description of iGEM see Brown (2007), Carlson (2010) and Cockerton (2011).

[3] Engineering and Physical Sciences Research Council.

new, and the collaborative partnerships were also, mostly, new. Indeed, given how young the discipline as a whole was, many of my participants were relatively new to academia as well, being either doctoral students or postdoctoral researchers. However, by the time I had completed my year of intensive fieldwork,[4] the people had settled in and gained experience and the rapidly growing Centre was in full swing. Alan Gregg, I came to learn, was an enthusiastic proponent of synthetic biology, espousing his vision of its golden future, a new industrial revolution, a route to resolving a wide range of human and environmental concerns from fuel shortages to bacterial infections, from contaminated water to cancer. Alan had seen the future and it was those "*ultimate manufacturing units*," cells. To his mind it was just a question of modifying them, tweaking their genetic code as you would a computer code, and plugging it back into the cell so that the cell would produce the desired product.

This vision for biology was, perhaps unsurprisingly, first championed by a group of engineers. These engineers were keen to see biology as simply the newest in a long line of engineerable materials, no different from any other if you just treated it 'correctly,' that is with logic and order, and thus got it under control. Amongst these early proponents were the two men Alan name-dropped in the quote above, Drew Endy and Randy Rettberg. Endy, a civil and biochemical engineer, and Rettberg, an electrical engineer, both worked with Tom Knight, regarded as one of the 'fathers,' if not "the godfather" (Bluestein 2012) of synthetic biology.

Knight, an electrical engineer by training, claims that he first became interested in combining engineering and biology after reading a proposal from physicist-turned-biologist Harold Morowitz. Morowitz reportedly claimed that if we put our minds to it and applied all of our advanced technology to biology, we could understand how simple organisms work (Bluestein 2012). Knight recalls his reaction to this proposal as follows:

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[4] I maintained intermittent contact with the Centre, and the field, for several more years after this period of intensive fieldwork.

"My general bias toward biology at that point was, oh my god, it's so complicated, we'll never figure out what's going on - in contrast to something like computers where you can understand everything. It was really quite amazing to see somebody proposing what I'd assumed was impossible. I got quite intrigued by the idea that I could go and do something with biology" (Knight quoted in Bluestein 2012).

Thus, prompted by the idea that he could "*go and do something with biology*," Knight reports that, sometime around 1990, he began reading classical biology books. Focusing in particular on simple organisms, which in turn led him to start sitting in on MIT's core undergraduate and graduate biology courses (Bluestein 2012).

In 1996 Knight used his growing understanding of biology to successfully apply to DARPA[5] for funding to pursue his interests in applying engineering knowledge to biology. It was during the tenure of his short term DARPA contract that Knight first set up a biology laboratory (Roosth 2010). The laboratory was located within MIT's Laboratory for Computer Science and was staffed entirely by non-biologists. It was here that Knight began to work on what he called, BioBricks. Standardised, well-characterised biological 'parts' that he envisioned could be used, like a biological version of Lego bricks, in the construction of more complex biological systems (Restuccia 2009; Roosth 2010).

Knight, Rettberg, and Endy,[6] were by no means the only early proponents of synthetic biology; they weren't even the only early proponents at MIT. However, due to their prominence in the beginnings of iGEM[7] and BioBricks,

[5] Defense Advanced Research Projects Agency.

[6] Knight has been called the "godfather" of synthetic biology, Rettberg now serves as the coordinator of iGEM and as manager of the registry of standard biological parts (the repository of BioBricks), while Endy has been described as synthetic biology's "most prominent spokesperson" (Rabinow and Bennett 2012: 21) and as the "figurehead and media darling of synthetic biology" (Roosth 2010: 54).

[7] Knight, Endy and Rettberg together started iGEM.

two early foundation stones of the discipline, and to repeated accounts of the early days of synthetic biology at MIT, their roles are written in synthetic biology lore. The fact that none of these three were trained in biology, and for that matter neither were other prominent early members of the synthetic biology community,[8] arguably played a large part in the early vision for, and approach of, the field.

Early visions of synthetic biology

The introduction of the engineering framework to biology, which this group of engineers ushered in, is perhaps most explicit in efforts to apply the engineering concepts of standardisation, abstraction, and decoupling to biology, and the assumed notion that novel organisms can be built from standardised, hierarchical parts, devices, and systems. According to Endy (2005), one of the most, if not the most, vocal proponents of the engineering approach to biology, standardisation implies that parts should be uniform and interchangeable, like screws or Lego bricks. It is believed that such standardisation of 'biological parts' would permit them to be interchanged and combined in new ways allowing the building of new biological organisms. Abstraction, the second of these core engineering concepts, has been drawn from computer engineering where it describes the reduction and factoring out of details within a frequently large and complex software system, or data structure, so that one can focus on a few concepts at a time. Within synthetic biology it is held that abstraction would permit the 'black-boxing' of the underlying biology allowing synthetic biologists to direct their efforts at producing novel biological 'parts,' 'devices,' and 'systems' without having to engage with the underlying DNA and its sequence of nucleotides (the As, Ts, Cs, and Gs). Lastly, decoupling denotes the separation of the design and fabrication processes. Within synthetic biology this would see workers specialised into two groups. Those who, with the help of computer modelling,

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[8] Including Chris Voigt (a chemical engineer), Gerald Sussman (an electrical engineer), Ron Weiss (an electrical engineer) and Robert Carlson (an aeronautical engineer).

design synthetic 'constructs,' and those who render these models as biological entities.

References to these engineering concepts, alongside the use of vocabulary and analogies drawn from engineering, are scattered throughout the synthetic biology literature, highlighting the pervasiveness of an engineering approach within the field (Arkin 2008; Baker et al. 2006; Endy 2005; Gibbs 2004; Serrano 2007). Indeed, much of the literature that describes and promotes synthetic biology claims that through the adoption of an engineering approach to biology, synthetic biologists hope to enable the design and construction of predictable, controllable living systems using well-defined, standardised, interchangeable parts (e.g. Endy 2005). It has been argued that in doing so synthetic biologists will, "learn about life by building it," make genetic engineering "worthy of its name"[9] and "stretch the boundaries of life and of machines until the two overlap to yield truly programmable organisms" (Gibbs 2004: 76). As I was to discover, Alan is far from alone in his belief that such controllable living systems could provide a solution to many of the world's ills, from water pollution to our reliance on fossil fuels, from expensive and imprecise pharmaceuticals to undetected bacterial infections (Ferber 2004a). He isn't even alone in casting synthetic biology as the next industrial revolution (Royal Society of Chemistry Science and Technology 2009; Schmidt 2008). Tom Knight himself is quoted as saying, in regards to synthetic biology's future:

> "I can't tell you what's going to happen. But stand back - this is the technology of the century. This is going to change how we build things. Biology is fundamentally a manufacturing technology, and we're on the verge of figuring out how to control that. It's impossible to predict and estimate the impact of that, but it's going to be massive" (Knight quoted in Bluestein 2012).

[9] Despite its name, genetic engineering does not apply an engineering approach to biology. As one of my research participants claimed "genetic engineering involves absolutely *no* engineering" (Malcolm, senior researcher, biology).

(Re)coining 'synthetic biology'

This potentially revolutionary advance however needed a name, one that alluded to both its biological and engineering pedigree. However, so the tale goes, at a *Nature* cocktail party in 2001 Drew Endy and Robert Carlson were still struggling to come up with a suitable title for the new discipline they envisioned (Campos 2009). Campos (2009) writes that Endy had discussed the notion of 'open source biology' with Carlson and Roger Brent in 1999, but the name, like another possible moniker 'constructive biology' hadn't stuck. 'Intentional biology,'[10] another option floated by Endy, had received a very bad reception, implying as it did that other approaches to biology, to which it was in contrast, were consequently 'unintentional.' So when the cocktail party came about, and they were still searching for a name, biophysicist Carlos Bustamante apparently suggested to Endy and Carlson that they use something analogous with 'synthetic chemistry.' Campos (2009) writes that this suggestion was not leapt upon immediately, Endy favoured 'natural engineering' for a time, but eventually 'synthetic biology' took hold, and thus the term was coined or, more accurately, 're-coined.'

It wasn't long before the realisation dawned that Endy and Carlson had not in fact invented the name 'synthetic biology,' or at least they were not the first to do so. Following this discovery, German biologist Barbara Hobom was frequently attributed with its coinage in 1980 (Hobom) (e.g. Benner and Sismour 2005; Chopra and Kamma 2006; Cuccato et al. 2009). While Balmer and Martin (2008) trace its introduction back further, to 1974 and the Polish geneticist Waclaw Szybalski (1974). However the sentiment that biology would soon be entering a "synthetic phase" was not, even then, a new one. As discussed in chapter six, we have appeared to be on the cusp of a 'synthetic biology' for a century, with the term being used by French biologist Stephane

[10] The Institute for the Future however seized upon the name 'Intentional Biology' and in 2006 published a report on this "new field" casting synthetic biology and biomimicry as its two main sub-fields (Pescovitz and Pang 2006).

Leduc as early as 1912. Yet there is no indication that Endy, Carlson, and Brent were even aware that their 'new' discipline, synthetic biology, had such historical namesakes.

But what does 'synthetic biology' actually mean?

Despite the effort and thought that went into naming synthetic biology, its appellation is not without ambiguity. Does the adjective 'synthetic,' as used in this context, infer that the biology in question is artificial, unnatural, man-made? Or does it imply that it is constructed, assembled, built? And what, for that matter, does this term say of 'biology'? Does the designation of the biology in question as 'synthetic' imply that other fields of biology are, by contrast, non-synthetic? And if so, does this imply that such biology is 'natural' in its constitution or 'organic' in its formation? Or, that the discipline of 'normal' biology, from which synthetic biology is a departure, focuses on analysis rather than synthesis?

There does indeed appear to be a shift in biology away from a focus on analysis and towards synthesis, towards designing and constructing organisms, and this shift is discussed in chapter six. However for now a clear definition for the discipline is perhaps needed. Given that, as highlighted by Evelyn Fox Keller (2009b), the ambiguity and multiplicity of meaning conjured up by the discipline's name indicates that it is perhaps less than obvious, to those encountering the term, what synthetic biology actually is. I have opted to use the European Commission's, New and Emerging Science and Technology, High Level Expert Group's definition, which describes synthetic biology as follows.

> "[T]he engineering of biology: the synthesis of complex, biologically based (or inspired) systems, which display functions that do not exist in nature" (NEST 2005: 5).

While arguably representative of the discipline as a whole, this broad definition nevertheless hides the fact that there is contention within the discipline over what this actually entails. Furthermore, it hides the fact that there are currently multiple strands of work going on under the label of synthetic biology.

Three approaches to synthetic biology

Amongst these strands of work are the three most common categories of approach to doing synthetic biology, namely the parts and pathways approaches, the genomes approach, and the systems approach. The parts and pathways approaches to synthetic biology are most clearly aligned with attempts to turn the field into an engineering discipline. Such approaches are underpinned by the assumption that simplicity is the key to achieving synthetic biology's aims, and that such simplicity can be achieved through adherence to, and the application of, standardisation, decoupling, and abstraction. Essentially, the synthetic biologists who adhere to these approaches are trying to build biological systems and organisms in the same way that you would build a machine, from standardised, controllable, well-characterised parts (O'Malley et al. 2007; Rabinow and Bennett 2008).

In contrast, the genomes approach to synthetic biology works at the whole genome level with the goal of determining 'minimal genomes' through the deletion of so called 'non-essential' genes. That is, genes that can be 'knocked out' without causing the death of the organism. This is being pursued with the aim of making simple, standardised 'chassis.' Chassis being the mechanistic term employed by synthetic biology to denote a cell/organism within which a synthetic biology system can be located and 'operated.' Currently the most common prokaryotic chassis is *E. coli* and the most common eukaryotic chassis is the yeast, *S. cerevisiae*. It is hoped that such chassis can be used as stripped down frames in which to 'assemble' desired synthetic genomes (O'Malley et al. 2007; Rabinow and Bennett 2008).

The most prominent example of this approach is the work of Craig Venter and his team.[11] In 1999 they announced the construction of a minimal genome

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[11] In embracing the genomes approach, it should be stressed, these synthetic biology's do not adhere to the parts-devices-systems approach promoted by Endy (2005). There approach is

for *Mycoplasma genitalium* (C. A. Hutchison et al. 1999), which the team called *Mycoplasma laboratorium*. While in 2016, having shifted their attention to *Mycoplasma mycoides*, they succeeded in produced a second synthetic, minimal cell, which they named syn3.0 (full name is JCVI-syn3.0)[12] (Clyde A. Hutchison et al. 2016).[13] Syn3.0 is, they claim, "a working approximation of a minimal cellular genome" being the result of a compromise between "small genome size and a workable growth rate" (Clyde A. Hutchison et al. 2016: 1414). Containing only 473 genes, syn3.0 currently has the smallest genome of any autonomously replicating organism (Clyde A. Hutchison et al. 2016).[14]

Finally, the third of the common approaches to 'doing' synthetic biology is the systems approach. This approach aims to construct minimal cellular systems, and to use "novel or modified natural systems to test and improve theoretical models of biological phenomena" (O'Malley et al. 2007: 59). It is also hoped that such systems will advance discussion around what constitutes life, and where the transition from non-life to life occurs.

While all three approaches are prominent within the burgeoning field of synthetic biology, and all are influenced by concepts and approaches from engineering, it is the first approach, the 'parts' approach, which has garnered the most attention. It is also this approach which is most prevalent within the Centre and within which the discipline's engineering approach is most explicit. As such, it is this approach that I shall focus on here.

The first synthetic biology papers

Nevertheless, despite their differences, all of these strands of synthetic biology are unified in their broad approach to biology. An approach that has been traced back, past the work of Knight and co. at MIT, to the work of

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arguably more similar to craftwork than to the industrial engineering-inspired approach promoted by Endy and embraced by the Centre directors.

[12] A name the ETC group have morphed into Synthia 3.0 (ETC Group 2016).

[13] syn3.0 was produced by transplanting a pared back version of the genome of *Mycoplasma mycoides* into a *Mycoplasma capricolum* cell which had be stripped of its own DNA.

[14] For comparison, the human genome contains more than 20000 genes.

Benner and Schultz. In 1989 these chemists constructed two artificial nucleotides in order to extend the DNA 'alphabet' from four 'letters' (A, T, C, G) to six (Gibbs 2004). Yet, as Gibb (2004) contends, the motivation for this work was grounded in science, rather than in engineering, pursuing as it did knowledge for the sake of illumination rather than for the purpose of application.[15] Synthetic biology as Keller (2009b) notes, and as shall be discussed in chapter four, is generally driven by the latter. Thus perhaps because of this difference in motivation, or perhaps because the work of these chemists was too early to be placed on the radar of young, newly fledged synthetic biologists, two papers from 2000 are more commonly cited as the first examples of synthetic biology to emerge. These papers by Gardner, Cantor and Collins (2000) and Elowitz and Leibler (2000) introduced two 'devices,' the toggle switch and the repressilator respectively.

These devices, designed to resemble electrical parts in terms of function, have had a significant influence on the subsequent work in synthetic biology (Gibbs 2004). This is despite the fact that both papers predated the term being (re)coined and thus are devoid of its mention and, for that matter, of any mention of the engineering concepts discussed above. Nevertheless both papers could be said to embrace an engineering approach to biology, and be focused on application, as subsequent synthetic biology work does.

Another early and influential, though much more controversial, paper was that by Cello, Paul, and Wimmer (2002). These three microbiologists synthesised the poliovirus by assembling oligonucleotides following instructions from the written DNA sequence of the virus. Following their success, the authors warned that "[t]here is no doubt that technical advances will permit the rapid synthesis of the poliovirus genome, given access to sophisticated resources" (Cello et al. 2002: 1018) and therefore that vaccination programs should remain vigilant in case bioterrorists seize such an

[15] According to Gibb (2004), Benner and Schultz, saw artificial genetics as a way of exploring basic questions such as the origins of life on earth and the potential for alternative forms elsewhere in the universe.

opportunity. Not surprisingly this contentious achievement spurred wide debate and discussion of the risks of synthesising pathogenic organisms. Including concerns that if these scientists could recreate a deadly virus using synthetic biology, so too could terrorist groups. Concern over biosafety[16] and biosecurity[17] was not however limited to the potential for rare pathogens, such as polio, to be synthesised in the lab. But rather extended to the potential for novel pathogenic agents to be designed, created, and released.

Discussing an uncertain future

This is the dark underbelly of all the hype about synthetic biology. The two sides of the synthetic biology coin, on one side of which are the potential novel organisms which will 'save the world,' and on the other, those that could cause death and destruction. The prevalence of discussions regarding the threat of such hypothetical adverse effects, is largely the work of certain activists, predominately those from the ETC Group. The ETC Group, a Canadian-based social activism group whose tag line is, "monitoring power, tracking technology, strengthening diversity" (ETC Group), have written extensively on synthetic biology. They have also written much about 'Synthia,' the name they gave to maverick synthetic biologist Craig Venter's so-called first synthetic organism (Gibson et al. 2010).[18] In these reports (ETC Group 2007, 2010), the ETC Group have arguably promoted the notion that synthetic biology's uncertain future, is more certain than it really is, and more problematic.

Jim Thomas, a programme director with the ETC group, for example, took Craig Venter's claims and promises regarding 'Synthia' at face value when he wrote: "[t]his is the quintessential Pandora's box moment - like the splitting of

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[16] Biosafety concerns the prevention of unintentional exposure to pathogens and toxins, or their accidental release.

[17]Biosecurity concerns the prevention of loss, theft, misuse, or intentional release of pathogens and toxins.

[18] As discussed in chapter five, Synthia has been the basis of a lot of discussion regarding the potential risks and benefits of synthetic biology.

the atom or the cloning of Dolly the sheep. We will all have to deal with the fall-out from this alarming experiment" (ETC Group 2010). Yet despite the disturbing comparisons and predictions made in this statement, as shall be discussed in chapter five, the significance of 'Synthia' has, according to those within the field, been overstated. Nevertheless, it is this mix of utopia and dystopia that has led synthetic biology to be called a dual-use technology. Consequently there is now a significant local and global focus on concerns around the potential unintentional or intentional release of harmful synthetic organisms, and the potential development of bioweapons.

Such a focus on synthetic biology's biosafety and biosecurity[19] issues is, in turn, part of a broader effort to achieve upstream engagement[20] with social scientists and the 'public' in regards to the field's so-called ELSI (Ethical, Legal and Social Issues/Implications). To this ends, funding agencies are increasingly requiring scientists to pair up with social scientists in order to receive grants. From a cynical perspective this situation may be motivating, or at least prompting, scientists' interest in forging such partnerships. Whereas from a social science perspective, the desire to address potential issues and implications early appears to be driven by the hope of subsequently influencing the development of the technology, and thus avoiding the scenario

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[19] Interestingly biosecurity has been of greater concern in the US than in Europe. Indeed, as Lentzos (2012) details, the US has been much more aggressive in addressing the security dimensions of synthetic biology. For example, the US Department of Health and Human Services (HHS) issued guidelines in 2010 for DNA synthesis companies to follow in screening both customers and their requested sequences. While the Recombinant DNA Advisory Committee proposed expanding the scope of the NIH Guidelines so that they would include synthetically produced nucleic acid molecules, and The National Science Advisory Board for Biosecurity (NSABB) have proposed a novel form of oversight for synthetic biology (NSABB 2010). In contrast concern in Europe has been focused on biosafety (Schmidt et al. 2008) with the European Commission calling, in 2005, for a review of the adequacy of existing safety regulations for managing engineered microorganisms and protecting against their inadvertent release (NEST 2005). In terms of biosecurity, the United Kingdom and the Netherlands stand out amongst the European countries for having considered the biosecurity aspects of synthetic biology in some detail, however unlike the US both have concluded that current regulatory frameworks are sufficient to address the risk of misuse (Lentzos 2012).

[20] That is a broad engagement with synthetic biology's ELSI before, rather than after, the science is fully developed.

whereby ethical and social assessment lags behind technological development (Deplazes et al. 2009).

To an extent this focus on ELSI is having a discernable impact on the discussion around and within synthetic biology, as well as on the field itself. 'Safety by design' has, for example, become a catchphrase. Indicating an effort to address bioerror and bioterror threats by 'designing in' safety features such as 'kill switches' and 'quorum sensing.' Features which would stop bacterial populations growing too big if they were released, or would prime them to 'self-destruct' once they had completed their task. However critics of this attempt by synthetic biologists to assuage ELSI-based critiques of the discipline argue that microorganisms by nature evolve and mutate. Therefore, there is no guarantee that such 'designed in' safety features would work.

A second catchphrase, 'responsible innovation[21],' has thus arisen in part as a response to the critique of safety by design.[22] 'Responsible innovation' indicates a belief that synthetic biologists not only need to include safety by design, but that they must also develop socially responsible products. Vincent (2013), however, vehemently questions this approach. Asking why each generation develops new technologies to rectify the damage caused by the last generation's new technologies without stopping to question their belief that their new technologies are safe and 'responsible.' She writes:

> "synthetic biology is often promoted as a source of technological fixes: biofuels meant to stop the overconsumption of fossile [sic] fuels, synthetic bacteria to repair the damages caused by chemical industries and nuclear power stations. But the concern with the damages due to the previous generations of 'new technologies' does not invite reflections about the next new generations, i.e. the long-term unintended consequences of all technological innovations. To

[21] Also termed responsible research and innovation (RRI)

[22] It is also at least an attempt at developing a strategy to address and assess not only the societal and ethical issues with synthetic biology but also its technical aspects. For a discussion of RRI in regards to synthetic biology see (Gregorowius and Deplazes-Zemp 2016).

be sure, the advocates of synthetic biology include risk assessment in their programs in the name of 'responsible innovation.' They earnestly address issues of biosafety and biosecurity in their annual conferences. Yet they only rely on technological solutions of confinement (physical, biological, evolutionary confinements), which in turn will raise new issues. Whatever the plausibility of the technical solutions for preventing the dissemination of and contamination by synthetic organisms, they never take into account past experiences, never draw lessons from the past" (Vincent 2013: 30).

Based on my observations of the field, I would agree with Vincent that the response of the synthetic biology community to the potential risks of their burgeoning field often leaves a lot to be desired. However, I would also acknowledge, as Deplazes et al. (2009) do, that much of the ELSI discussion around synthetic biology is based on speculation. Exploring as it does the potential impacts of future applications, and as yet unrealised scientific and technological advances.

Furthermore, such speculation, as Deplazes et al. argue, can be grounded on "exaggerated hopes or unnecessarily bleak scenarios" (2009: 68). Indeed, it could be argued that the visions of Alan, and Tom Knight, for the gilded future of synthetic biology fall into this former category. While the concerns of the ETC Group, that advances in synthetic biology will see the design, creation, and release of dangerous organisms and/or novel pathogens, arguably fall, at least currently, into the latter category. Tucker and Zilinskas for example argue that such a scenario is "extremely unlikely" (2006: 38). While Lentzos (2009, 2012) points out that making bioweapons is actually incredibly difficult and that, at least at present, terrorists do not have the capability to develop such weapons using synthetic biology.[23] Yet despite the speculative nature of

[23] Some critics have therefore argued that the focus of biosecurity concerns should consequently centre on military uses of synthetic biology rather than potential terrorist uses (Lentzos 2009). Considering, perhaps, that before it was shut down in 1969 the US bioweapons program had succeeded in weaponising and mass-producing agents that would

such visions of a dystopian future, just discussing them with any seriousness bears risks. For, as Lentzos et al. write,

> "there are also hazards in imagining and describing the future in a certain way; particularly when certain technological trajectories (and the actions of certain social groups) are presented as inevitable. The reason being, once spoken, there is a tendency to conceive of such scenarios as real, imminent, and in need of action on the part of scientists, regulators, concerned interest groups, and others" (2012: 135).

Yet such a hypothetical, future-oriented focus is common in many of the current 'ELSI' discussions around synthetic biology. Not just in relation to biosafety and biosecurity (e.g. Kelle 2007, 2009; Schmidt 2008, 2010) but also in regards to intellectual property (IP) and patenting (e.g. Bhutkar 2005; Kumar and Rai 2007), the future governance of synthetic biology (e.g. Kelle 2007; Weir and Selgelid 2009), and global equity of access to partake in the science and the equitability of its products (e.g. Deplazes et al. 2009; Wellhausen and Mukunda 2009). Such discussions are both interesting and potentially very important, given that without them there is a risk of the social and ethical discussions running behind the science. However, such discussions can, as we saw with the disconnect between the biosecurity concerns and the scientific reality, instead run ahead of the science and thus be out of step with the current reality of the science.

In the case of IP and patenting, concerns around patent thickets and anti-commons developing within synthetic biology, while worthy of discussion, are more representative of potential future scenarios than the current situation. While the discussions around global equity, an issue of great potential ethical import, are arguably also a little premature given that only a handful of

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cause anthrax, tularemia, brucellosis, Q-fever, Venezuelan equine encephalitis, and botulism (Croddy 2000).

products have so far been brought to market.[24] Such ELSI discussions are, therefore, based on various hypotheses and possible scenarios, rather than on the scientific reality. A situation which led Vincent (2013) to claim that ethicists and activists (she does not mention other social scientists) are so caught up in their own imagined futures that they are missing the chance to formulate a meaningful critique of the promises of synthetic biology.

Tait (2009) is likewise critical of the ELSI process, using the gap between these ELSI discussions and the current reality of the science, to dispute the inherent usefulness of upstream engagement. While I recognise the gap Vincent and Tait address, I would nevertheless disagree with Tait on this point. Upstream engagement, I would contend, is potentially very valuable, but future-focused discussions should not be the sole pursuit of such engagement. Rather, like Marris and Rose (2012), I would argue that a valuable part of such upstream engagement is the close involvement of social scientists and synthetic biologists as the field develops. As Marris and Rose (2012) address, an important way of achieving this desired involvement is through embedding social scientists within the field as it develops. While such involvement can bolster discussions of the synthetic biology-specific ELSI, which are more grounded in the current reality of the science's progress, it can also lead to a greater understanding of the progress and process of the day-to-day science itself. It was this latter prospect which most interested me. For, while I acknowledge the importance of discussions of biosafety, biosecurity, intellectual property, governance, and global equity, I am myself more interested in what is actually happening within the developing discipline on a day-to-day basis. And how the synthetic biologists themselves think about the field, its processes, promises, problems, and potential products.

[24] For example, Jay Keasling's synthetic version of the anti-malarial drug Artemisinin has only recently been brought to market, and while it may indeed cause issues, it is still too early to say what impact it will have in terms of equity with any degree of certainty.

Central research questions

With these interests in mind the central aim of this research project was to explore the interactions between engineering and biology, and thus between engineers and biologists, within the burgeoning field of synthetic biology. In doing so, the project investigated the following overarching research questions:

- Synthetic biology is framed as a hybrid discipline of biology and engineering. However, these parent disciplines bear significant differences in education, knowledge base, approach, language, and methods. Therefore, how can we think about, and make sense of, the relationship between synthetic biology's constituent, but divergent, 'halves'?[25]
- How does the relationship between engineering and biology manifest itself in the day-to-day workings of synthetic biologists, and what does it mean to attempt to 'engineer biology'?
- What impact does applying an engineering framework to biology have on the synthetic biologists' understandings of the 'products' of their work?
- How does synthetic biology (and indeed previous efforts to integrate biology and engineering) fit into the broader history of attempts to investigate and shape the biological world? And can synthetic biology be thought of as part of an attempt to 'do' and think of biology differently?

In order to pursue these questions I undertook a twelve-month ethnographic study within the Centre mentioned at the beginning of this chapter, the details of which are discussed in chapter two. Chapter two also provides a portrait of the Centre itself and addresses some of the issues I faced in gaining acceptance into the field and ultimately leaving it. Interestingly, despite the relative openness of synthetic biology to collaboration with social

[25] I shall address my rationale for speaking of synthetic biology as consisting of two 'halves,' or being made up of two 'groups,' in chapter three.

scientists, ethnographies of the day-to-day practices of this community are so far rare. As such this thesis is a significant contribution to this growing literature (Calvert 2010a; Cockerton 2011; Molyneux-Hodgson and Meyer 2009; Rabinow and Bennett 2012; Roosth 2010). It also draws on, and contributes to, literature on the social aspects of synthetic biology (e.g. Balmer and Martin 2008; Calvert 2008; Frow and Calvert 2013; Keller 2009b; Lentzos 2009; Lentzos et al. 2012; O'Malley et al. 2007; Rabinow and Bennett 2009; Schmidt et al. 2009), as well as the rich body of ethnographies that explore the practices, impacts, and implications of science and engineering (e.g. Bucciarelli 1994; Downey 1998; Knorr Cetina 1999; Latour and Woolgar 1979; Rabinow 1996, 1999; Traweek 1988; Vinck and Blanco 2003).

Theoretical framework

Synthetic biology is, as discussed above, an emerging hybrid discipline, which combines the disparate disciplines of biology and engineering, and which raises a wide array of social, ethical, philosophical, and scientific questions. As such, there are many bodies of sociological and STS literature within which a study of synthetic biology could find a home, and which I could therefore draw upon to investigate the above questions. For example my research interests led me to explore historical literature addressing the beginnings of synthetic biology in both its current incarnation and the incarnations of its historical namesakes. Delving into the stories of these previous 'synthetic biologies' subsequently led me to literature that explores the broader histories of biology (e.g. Bud 1993; Caron 1988; Gottweis 1998; Haraway 2004; Kay 1993, 1995, 2000; Keller 2000; Wright 1994), and engineering (e.g. Anderson and Tushman 1990; Buchanan 1985; Divall 1990; Hill 1984; T. Hughes 1983; Noble 1977; Vincenti 1993), and ultimately that of previous attempts to take an interventionalist approach to biology and thus understand biology in engineering or mathematical terms (e.g. Bud 1993; Compton and Bunker 1939; Keller 2002; Keller 2009b; Leduc 1910, 1911, 1912; Loeb 1912; MIT ; Pauly 1987; Rashevsky 1938; Rasmussen and Tilman 1998; Sourkes 1955; Thompson 1961; Turing 1952; Wright 1994). However, I have ultimately chosen to explore synthetic biology as a case study of a new way of thinking about and interacting with biology.

Given the nature of what synthetic biology is attempting to achieve – the hybridisation of ideas, language, techniques, and indeed people from biology and engineering in order to render biology, and thus life, engineerable – the discipline itself and thus a case study of it, ultimately possess both practical and conceptual components. That is, both practical and conceptual factors must be considered in order to answer the question, and simultaneously the problem, which synthetic biology both poses and faces - how does one endeavour to engineer life? Practically speaking, synthetic biology is attempting to address this problem by forging a new discipline using the skills and expertise of both biologists and engineers. Thus the following case study, which highlights the conflicts and compromises inherent in this exercise in discipline building, draws from and contributes to the sociological and STS literature on interdisciplinarity and discipline formation. Whereas conceptually, synthetic biology's notion that life is engineerable, that it can be thought of, and manipulated to become, stripped back, modular and standardised, links this case study to the STS literature on reductionism. In order to locate this study within these broad bodies of literature I shall first briefly discuss them in turn.

Interdisciplinarity

The term interdisciplinarity, as Klein (1990) discusses, has been in common usage since the latter half of the twentieth century and broadly refers to various attempts and desires to "integrate different perspectives" (1990: 15). However, as Klein makes clear, its definition remains contested. Indeed, it would seem that all cross-disciplinary practices, including multidisciplinary, interdisciplinary, and transdisciplinary working, have multiple and contested definitions (see for example Aboelela et al. 2007; Callard and Fitzgerald 2015; Stock and Burton 2011; Van den Besselaar and Heimeriks 2001). Thus, perhaps because of this lack of clear definitions, and what Frickel et al. (2016) describe as the plasticity of meaning surrounding interdisciplinarity, and its status as a boundary object, 'interdisciplinary' is often taken to be an umbrella term for all forms of cross-disciplinary practice (Barry et al. 2008; Heimeriks 2013). Nevertheless, regardless of terminology there seems to be a general consensus that there has been an increasing shift towards interdisciplinarity in recent decades.

While Klein (1990, 1996) provides a useful and detailed history of interdisciplinarity, linking it back to its historical antecedents, most sociological literature on this subject focuses instead on measuring and discussing the nature, benefits, and challenges of implementing various cross-disciplinary working relationships. Indeed one prominent theme within this literature addresses the formation of interdisciplinary collaborations (see for example Derry et al. 1998; Klein 1996) and the barriers that need to be overcome in order to allow them to form (see for example Bauer 1990; Casey 2010; Frodeman et al. 2010; Klein 2010; Laudel and Origgi 2006; Lélé and Norgaard 2005; Öberg 2009; Repko 2012; Winowiecki et al. 2011). Another key theme is the development and/or exploration of various ways of measuring, assessing, and evaluating the resultant interdisciplinarity of such teams (see for example Huutoniemi et al. 2010; Morillo et al. 2003; Porter and Rafols 2009; Rafols and Meyer 2010; Van den Besselaar and Heimeriks 2001). While others, such as Rhoten (2003), Strathern (2005), and Mansilla (2006), argue that the most important features of interdisciplinarity defy such measurement.

What arguably underlies much of these discussions of interdisciplinarity is the assumption that it is, itself, a positive research goal. Indeed much is made of interdisciplinarity being both an antidote to the shortcomings of traditional disciplinarity,[26] and a panacea for research into all our contemporary social, environmental, and political ills (Lawrence 2010; National Science Foundation. Directorate for Social 2011; Stock and Burton 2011; Stokols 2014). Such

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[26] Understood as being the assembling of sets of elements, such as "objects of study, methods of analysis, scholars, students, journals and grants" (Messer-Davidow et al. 1993: 3) into distinct disciplines which become embodied in institutions, systems of training, and canons of work which in turn set the frameworks for the kinds of questions and answers each discipline pursues.

assumptions have lead to discussions regarding the relative benefits of interdisciplinarity and disciplinarity (see for example Austin et al. 2008; T. R. Miller et al. 2008), and of Mode 1 vs. Mode 2 knowledge production (Heimeriks 2013). Discussions which, arguably, tend to be uncritically positive about interdisciplinarity while portraying disciplinary work as homogenous, oppressive and closed (Frickel et al. 2016). On this note Frickel et al. (2016) contend that discussions of interdisciplinarity tend to be underpinned by unquestioned assumptions regarding disciplinary and interdisciplinary research. Assumptions which posit that interdisciplinary research is better; that disciplines are silos which constrain the development of interdisciplinary knowledge; and that interdisciplinary interactions are free of the status hierarchies and power dynamics common within disciplines (Frickel et al. 2016). Frickel et al. further argue that insufficient attention has been paid to the pressure put upon institutions and researchers to embrace interdisciplinarity, and the long-term impacts such pressure will have on education and research landscapes.

Like Jacobs and Frickel (2009), and Klein (1996), Frickel et al. (2016) thus turn the spotlight on this assumption by exploring the wider institutional and political context of interdisciplinary activities. With this focus, Frickel et al. (2016) argue that interdisciplinarity is currently encouraged and incentivised from both within and outside of academia, driven by political and economic interests, as well as academic interests. According to these authors, this "insistent and sustained push from administrators, policy makers, and funding agencies to engineer new research collaborations across disciplines" (Frickel et al. 2016: 5) is seldom acknowledged.

Bauer likewise highlights the too frequent lack of critical analysis of interdisciplinarity, writing that, "[l]ike any new venture, an interdisciplinary one must demonstrate its value and not expect to be appreciated before that event" (1990: 113). While Barry et al (2008) argue that contrary to the sorts of assumptions Frickel et al. (2016) outline as being prevalent in the literature, disciplines and interdisciplines can be equally closed or open, internally divided or homogeneous. A point supported by Heimeriks (2013) who likewise argues that the contrasts between disciplinary and interdisciplinary research are not always convincing.

Nevertheless despite the valid criticisms of the way interdisciplinarity is often viewed as an unquestioned good, Barry et al. (2008) assert that it is not just political impetus that is currently driving interdisciplinarity. Rather, they contend that irrespective of the political and institutional pressures, interdisciplinary research does have the potential to be inventive and open up new possibilities. To evidence this point, the authors highlight that interdisciplinarity is far from a new phenomenon, having been responsible for the development of many, now established, disciplines. What Barry et al. (2008) argue is new about the current trend in interdisciplinarity is the demand that research be better integrated into society and the economy. This outcome is sought through the development of interdisciplinary relationships between science/engineering and social sciences/arts/humanities. Thus, it is now expected that interdisciplinary projects will ensure that science is accountable to society and that scientific research leads to economic growth. Nowotny et al. (2001) and Strathern (2005) likewise address the relationship between the drive towards interdisciplinarity and the increasing demand for science to engage with society. While Strathern particularly focuses on how this political drive affects those charged with facilitating such interdisciplinarity. A study which leads her to note, rather pithily that, “[t]here is nothing straightforward about bringing together disciplines” (Strathern 2005: 82).

Discipline formation

Given synthetic biology’s goal of bringing biology and engineering together, and the pressure synthetic biologists are under to engage in collaboration with social scientists, the emerging discipline arguably classifies as an interesting case of interdisciplinarity. Thus there is, undoubtedly, a story to be told about the political dynamics and institutional pressures driving the formation and advance of synthetic biology (such as the way Lenoir (1993) explores discipline formation). Indeed, the degree and type of interdisciplinarity the field is achieving is certainly ripe for analysis. Yet, while such stories would be interesting, I have chosen instead to focus on how the impetus for novelty and invention, acknowledged by Barry et al. (2008), can drive the formation of new disciplines and research communities. As Etzkowitz writes, "[d]iscipline formation through synthesis is the next step beyond the phenomenon of interdisciplinarity. There has been a shift in knowledge organization from creating a discipline by splitting it off and differentiating it from an old discipline . . . New disciplines are more recently created through synthesis" (2003: 327). By which he means integrating elements of different disciplines into a new discipline.

Synthetic biology is, I would argue, just such a project to create a discipline through synthesis. Thus, in exploring the early days of the Centre's existence and its inhabitants' attempts to realise this project, this thesis is a case study of such a strategy, or indeed a range of strategies, to create a new discipline. And the most interesting thing about this new discipline, I would contend, is that it is being formed around the aspiration for application. That is, it is driven by the desire to do things differently in order to produce a new knowledge base and new entities for biotechnology. In this way it is not alone. Indeed, as shall be discussed in chapter six there are a growing number of new disciplines emerging at the intersection of biology and engineering which are also driven by this aspiration for application (examples include neuro-engineering, tissue engineering, nanobiotechnology, and genome engineering).

In exploring synthetic biology in this way I draw on the work of Molyneux-Hodgson and Meyer (2009), Swazey (1992), Clarke (1998), Leonelli and Ankeny (2015), Star (1999), Powell et al. (2007), Fujimura (1987), Clarke and Fujimura (1992), and Knorr Cetina (1999) among others. Swazey's (1992) work on the Neuroscience Research Programme, for example, provides useful insight into the ultimately successful project to create the discipline of neuroscience, a subject also addressed by Rose and Abi-Rached (2013). Given that neuroscience is, as Swazey details, a discipline forged out of the fusing of "historically disparate disciplines" (1992: 529), this project bears similarities to that of synthetic biology. Similarly I draw on Clarke's (1998), exploration of the formation of the discipline of reproductive science, as this too details the bringing together of incongruent disciplines (biology, medicine, and agriculture) in order to study life differently. Disciplines, Clarke asserts, "mark territories and usually seek to do so vividly" being "simultaneously constitutive and controlling" (1998: 7). Thus disciplinarity is ultimately, she notes, quoting Messer-Davidow, Shumway, and Sylvan, "about the coherence of a set of otherwise disparate elements: objects of study, methods of analysis, scholars, students, journals, and grants to name a few." It is "the means by which ensembles of diverse parts are brought into particular types of knowledge relations with each other" (Messer-Davidow et al. quoted by A. Clarke 1998: 15), and it is these relations that become the objects of study for those studying discipline formation.

Given synthetic biology's wide array of inter-relating and diverse parts, it is important to clarify my particular point of focus. As Clarke quite astutely acknowledges, sociology asks the simple, yet pivotal, question regarding any given research project: "What is this a story of?" (1998: 273). Thus, much like Clarke's (1998) answer to this question, regarding her work on the formation of reproductive science, I would answer as follows. This thesis contains many genres of story. Stories of the formation of a research centre, stories of conflict and compromise for those involved in its emergence, and stories of conceiving, and struggling to conceive of life as engineerable. However, just as Clarke did, I would ultimately contend that this is primarily a story of a project to control life. Clarke's examination of life took place at the complex organism level – humans, lab species, and agricultural animals – and focused on the way life is controlled through the rationalisation and industrialisation of reproductive processes. Thus, by contrast, my object of study, synthetic biology, is a project to establish a discipline with the expressed aim of controlling life at a molecular level.

There are subsequently two parts to this story, firstly the work to establish the discipline, and secondly the work to bring to fruition the goal of the discipline. In terms of the first of these, the literature on discipline formation provides a list of factors that are deemed important in the successful establishment of a discipline, and which I shall address in regards to synthetic biology in the following chapters. Powell et al. (2007), for example, address the need to name a new discipline, to give it a label that those involved can coalesce around and identify with as they carve out their territory. A name, they argue, demarcates an area of epistemological territory while conferring "unity on highly diverse scientific activities and aims" (Powell et al. 2007: 07). However it cannot be just any name. Rather, Powell et al. argue that choosing the 'right' name is of the utmost importance. For it must connect with both the developing research activities and the problems of the discipline. While also acting as "a marketing tool" by "announcing some sort of progress to the world outside the pertinent scientific community" (Powell et al. 2007: 18).

Clarke (1998) and Swazey (1992) likewise address the importance of naming in establishing and maintaining such boundaries, however Swazey argues that it is not always straightforward to establish such a moniker. In their search for the 'right' name, the endeavour to form neuroscience, she highlights, underwent several name changes before settling on the Neuroscience Research Program (NRP). As detailed above, synthetic biology likewise went through several proposed names before one was settled on, and while it is still controversial, the growth of the discipline suggests that 'synthetic biology' is proving successful as a label around which people will coalesce.

According to the literature, another important factor in the formation of a new discipline is the need for constructive, cohesive, and collaborative relationships between those involved. Swazey (1992) writes of the importance of such relationships in the success of the NRP, noting that they allowed those from divergent backgrounds to communicate and work together as neuroscientists. Clarke (1998) also addresses the importance of collaboration but, the form of collaboration she studied differs significantly from that within neuroscience, and indeed synthetic biology. Where the participants in neuroscience coalesced to such a degree that they formed a reasonably coherent and cohesive discipline, those that Clarke studied, within the reproductive sciences, shared a common research object but stayed relatively separate within, what she terms, "distinctive subworlds" (1998: 149) (located within biology, medicine, and agriculture). While there are significant differences between these two versions of interdisciplinary collaboration,[27] in chapter three I contend that we can think of them using an analogy of different kinds of intercellular interactions.

A further important component in the establishment of a discipline, as addressed in the literature, is infrastructure. Ankeny and Leonelli (2011), for example, explore the importance of infrastructure to the development and function of model organism communities, while Swazey (1992) discusses its importance to the establishment of neuroscience. Swazey also notes however that such infrastructural components as research centres, conferences, funding streams, and journals are factors that have long been key to the establishment of research communities. Yet, despite the central role of infrastructure in the establishment and functioning of research communities, Star (1999) acknowledges that such "hidden mechanisms" of processes, are often considered "boring."

Star nevertheless spent a great deal of effort ethnographically studying such 'boring' elements and ultimately established, with Ruhleder, a detailed definition of infrastructure and its necessary properties (Star and Ruhleder 1996). Included in this list of properties is the requirement that infrastructure is "learned as part of membership" (Star and Ruhleder 1996: 113). New participants within a community of practice, the authors assert, must "acquire a naturalized familiarity with its objects as they become members" (Star and Ruhleder 1996: 113). Such a familiarity, Swazey details, can be attained through the "re-education" of those involved with a discipline-formation project.

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[27] It should be noted that the interdisciplinary collaborations often studied by those exploring interdisciplinarity are temporary research networks, which draw individuals from different fields. These require shared language, research objects, communication, and cooperation but the contributing disciplinary boundaries remain. The kinds of collaboration I am exploring here, and indeed that of synthetic biology are different. In these cases it is not a network that they are seeking to create but a new discipline, and this, I would argue requires a deeper level of collaboration.

In regards to the NRP, Swazey writes that such a strategy laid the groundwork for the training of a new generation of neuroscientists by allowing those involved to "begin transmitting new, interdisciplinary ways of thought and work to colleagues and students at their own institutions, helping to propagate a new genealogical tree of neuroscientists that did not exist a generation ago" (Swazey 1992: 542). The importance of training students in a transdisciplinary way, in order to prepare them to work in the collaborative manner mentioned above, is further discussed by Stokols (2014). While, Powell et al. (2007) would add to this list of features of developing disciplines, the need for a proof of principle, an experimental result that clearly demonstrates the viability of the discipline. In regards to synthetic biology, the two founding experiments described above, the repressilator (Elowitz and Leibler 2000) and the toggle switch (Gardner et al. 2000), have arguably acted as such a proof of principle for the discipline.

The importance of such a collection of features to the process and success of discipline formation is broadly discussed by Clarke (1998), who examines the ways in which a research community remains interactive, coherent, and viable over time and changing circumstances. Here Clarke takes a step back from the particular features themselves to note that the reproductive sciences arose at a time when the right combination of factors in the professional, scientific, institutional, and activist social worlds came together. In Clarke's work it seems that the most important thing to the success of the reproductive sciences was not that the factors appeared but that they appeared together. Similarly, Molyneux-Hodgson and Meyer explore the emergence of synthetic biology, focusing on the core elements of the formation of the research community in terms of, what they term, 'movement and stickiness.' While their approach to exploring synthetic biology is useful, and is discussed in chapters three and four, it also brings to mind Leonelli and Ankeny's (2015) notion of repertoires and Fujimura's (1987) notion of doability to which I shall now turn.

Repertoires, doability, and epistemic cultures

As shall be discussed in chapter four, Leonelli and Ankeny (2015) examine the material and social conditions under which research communities are created, managed and persist in the long term. Addressing the process through which short-term research projects acquire the resilience and flexibility to evolve into active, productive scientific communities, the authors conclude that a group must develop what they term a 'repertoire.' A repertoire, being a distinctive and shared ensemble of skills, behaviours, methods, and resources (such as those listed above), that both draw a community together and which can be used to train newcomers. Their focus on practice here is significant as Leonelli and Ankeny, like Kuhn (1962), Clarke (1998), and Knorr Cetina (1999), reject the notion that shared theories are the core constitutive factor of a discipline or field. Instead they argue that, while theoretical insights and disagreements are important, some research communities develop in the absence of common theories, being drawn together instead by common practices and infrastructure.

Essentially then, the development of a repertoire is, Leonelli and Ankeny assert, "an important moment in the growth of a scientific community, in which key goals and values come to be explicitly articulated and efforts are aimed at making it feasible to achieve these goals, often through the inclusion of new groups and approaches" (2015: 707). Where Leonelli and Ankeny refer to this "important moment" as the development of a repertoire, Fujimura would call this the moment when a problem becomes 'doable.'

According to Fujimura (1987), scientists tend to pursue problems that they consider 'do-able' at three key levels. At the experiment level, she argues, there needs to be well-defined tasks which can be carried out to address the problem. At the laboratory level such experiments must be prioritised and the necessary equipment to undertake them must be available. While at the social world level there needs to be a secured funding stream to finance the laboratory equipment and the experiments, and also conferences and journals to disseminate any results. Doability, Fujimura (1987) stresses, is thus not just a technological issue, but also a social issue. As such, she explores how doability is manifest in the actual work processes of scientists, the conditions under which problems are made, or deemed to be, doable, and the way in which doability can be constrained.

Part of the articulation work, Clarke and Fujimura (1992) identify as being integral to the construction of a doable problem, is the alignment of experimental work with the concerns of both academic and commercial audiences in order to draw resources from both worlds. This need to align a research problem across multiple worlds is also addressed by Clarke who, drawing on Fujimura's work, argues that doability equates to scientists assessing whether or not a specific line of work "is feasible and worthwhile to undertake at a specific time and place" (1998: 85). The feasibility, and thus doability, of a line of work, Clarke contends, is reliant on investigators aligning their research problems "across experimental capacities, laboratory organization and direction, and the broader worlds of fiscal, scientific, and extrascientific support" (A. Clarke 1998: 85). Thus Clarke notes that she "would extend Fujimura's definition to assert that doability generally implies some kind of profitability" (1998: 89) and practical output.

The need for practical output is also acknowledged by Clarke and Fujimura when they write, regarding achieving doability that, "[b]efore beginning the work, scientists must both pull together and articulate – craft the necessary connections among – a wide array of requisite elements to make as sure as possible, given local and other circumstances, that something they think will be recognized as worthwhile by significant others will emerge downstream" (1992: 8). Thus, according to Fujimura and Clarke (A. Clarke and Fujimura 1992; Fujimura 1987), a scientific problem must be technically doable at the experimental level, prioritised at the laboratory level, and furnished with the necessary infrastructure, funding, and support at the laboratory and social world levels in order to be truly doable.

Thus looking at this work on discipline formation more broadly, the creation of a discipline arguably requires the social, conceptual, and material components of a repertoire. Which is, in turn, a necessary component within the broader strategy of rendering an emerging discipline's research problem doable. A strategy which, as Fujimura and Clarke describe (A. Clarke and Fujimura 1992; Fujimura 1987), requires a lot of articulation work, and the alignment of factors across the experimental, laboratory, and social world levels. However, I would add another layer of analysis here. Indeed, as I shall argue in chapter four, establishing a robust repertoire and a doable problem for an emerging discipline are key factors in the formation of that discipline's epistemic culture. Epistemic culture being a concept developed by Karin Knorr Cetina (1999), and investigated in chapters three and four.

As shall be discussed in chapter three, Knorr Cetina's (1999) notion of epistemic cultures was developed to make sense of the differences between scientific disciplines and the ways in which they create, and assess, knowledge. The concept was not, therefore, developed as a tool for exploring discipline formation. However in exploring the concepts of repertoire and doability described above, I became aware of the similarities between these notions and that of an epistemic culture's epistemic machinery. All three concepts address the social, conceptual, and practical aspects of a scientific endeavour. However, where repertoire and doability address the importance of these factors in the formation of a scientific community, Knorr Cetina asserts that such factors become part of the distinct epistemic culture, which defines and cements an established community. Thus, in examining the first part of the story of synthetic biology, the work to establish the discipline, I draw on the ideas of repertoire and doability in order to explore how a hybrid research community, can successfully create a distinct hybrid epistemic culture for its developing discipline.

Exploring synthetic biology's formation

Chapter three thus addresses the first of the research questions listed above. Exploring how we can think about, and make sense of, the relationship between synthetic biology's constituent, but divergent, 'halves.' Synthetic biology is frequently framed as the unproblematic collaboration between biologists and engineers intent on creating a hybrid discipline. Thus in terms of the discipline's repertoire, it would seem that the necessary constructive, cohesive, and collaborative relationships have emerged smoothly, and without tension. Yet, as I discovered during my fieldwork, this is not an accurate depiction of the day-to-day reality of synthetic biology. Rather those within the field are seen as belonging to one 'side' of the discipline or the other, and these 'sides' clash and conflict due to their vastly different expectations, understandings, and approaches. In order to make sense of these differences, I draw on the work of Knorr Cetina (1999), and her notion of epistemic cultures, casting biology and engineering as differing, yet interacting, epistemic cultures.

Yet, despite the conflict and tension between the differing epistemic cultures within synthetic biology, I also witnessed a commitment to collaboration and compromise within the Centre, and an embracing of explanatory pluralism (Keller 2002), in order to 'make it work.' As discussed in chapter three, for some within the Centre this desire to bring the two sides of synthetic biology together was expressed through their commitment to close, collaborative working relationships. While for others it was evident in their dedication to becoming interdisciplinary individuals, as described by Eddy (2005). Eddy's notion of interdisciplinary individuals is also drawn upon in chapter three in order to explore the role that training and education are playing in the development of the discipline of synthetic biology. Other elements of the discipline's developing repertoire, and thus epistemic culture, are discussed in chapters two and four. Chapter two touches on the establishment of the Centre's infrastructure, and chapter four explores the Centre's attempts to establish both conceptual and practical norms.

Given their commitment to 'making it work,' and to embracing both collaboration and the discipline's engineering approach, in chapter four I address my second research question: how does the relationship between engineering and biology manifest itself in the day-to-day workings of synthetic biologists, and what does it mean to attempt to 'engineer biology'? Indeed applying an engineering approach to biology is the problem that synthetic biology is attempting to make doable. Thus, by exploring what taking an engineering approach to biology actually means to synthetic biologists, and how it affects the ways in which they talk about, think about, and undertake their work, chapter four examines the day-to-day practices of attempting to render a research problem doable, and thus establish a epistemic culture for the discipline. I found that the adoption of an engineering approach to their work was strongly promoted by the directors of the Centre, and was embraced by most of those who worked within it, who were equally keen to distance their discipline from biology. This commitment to seeing life as engineerable was most clearly manifest in the members of the Centre's adoption of an efficient, rigorous, and logical approach to their work. An approach drawn from an idealised notion of what engineering is, and evident in the language used, the questions asked, and the experiments run. Yet, despite their commitment to this engineering approach, enacting it in practice was not, as chapter four addresses, without obstacles.

This leads us on to the second part of this case study's story, the work done to bring the goal of synthetic biology to fruition. Synthetic biology, as mentioned above, and examined in chapter six, is embracing the notion of life as engineerable material, yet this notion requires the enactment of a heavily reductionist approach to biology. As such I shall now turn my attention to the sociological and STS literature on reductionism.

Reductionism

Reductionism, much like interdisciplinarity and discipline formation, has been the subject of much debate and discussion within the STS literature. As is examined in chapter six, Descartes introduced the idea of reductionism in the seventeenth century. He argued that the world was like a machine, and its pieces like clockwork mechanisms. Thus the machine, he contended, could be understood by taking the pieces apart, studying them, and putting them back together to see the bigger picture (Descartes 1988). In other words, he proposed that, in essence, reductionism is the belief that you can reduce the whole to its parts, it being no more, and no less, than their sum, and thus a chain of causation exists from the parts to the whole (Lewontin et al. 1984). Ernest Rutherford, for example, is famously quoted as saying that "all science is either physics or stamp collecting" (Blackett 1962: 108). Asserting that, ultimately, all scientific phenomena could be accounted for by their basic physical components. A remark which, Hayes (2004) claims, did not win physics many friends among practitioners of the other sciences.

Nevertheless despite such resistance, Gallagher et al. (1999) contend that the predominant approach used to relate the different fields of science to one another is still reductionism. While biologists have traditionally been, and arguably remain, the most resistant to such reductionism (Grene 1987; Nagel 1998; Alexander Rosenberg 2008), as Van Regenmortel (2004) and Rosenberg (2008) detail, with the advent of molecular biology some biologists began embracing this approach. Francis Crick, for example, reportedly claimed that, "[t]he ultimate aim of the modern movement in biology is to explain all biology in terms of physics and chemistry" (quoted in Van Regenmortel 2004: 1016). The theory, Van Regenmortel claims, goes as follows: "because biological systems are composed solely of atoms and molecules, without the influence of 'alien' or 'spiritual' forces, it should be possible to explain them using the physicochemical properties of their individual components, down to the atomic level" (2004: 1016). Yet, as Van Regenmortel also addresses, it has equally been argued that reductionism has its limits, limits which antireductionists have seized upon in order to "regard biology as an autonomous discipline that requires its own vocabulary and concepts that are not found in chemistry and physics" (2004: 1016).

Antireductionism

Antireductionism is, therefore, a philosophical position that stands in contrast to reductionism, advocating that not all properties of a system can be explained by examining its simplest constituent parts and their interactions. Such an argument over whether the whole is, or is not, merely the sum of its parts, has fuelled many debates and discussions of the topic, both by those within and outside of the life sciences (see for example Canguilhem 2009; Hoyningen-Huene 1992; S. Rose 1997; N. Rose 2013; Alex Rosenberg and Kaplan 2005; Van Regenmortel 2004). Debates, that is, which have spanned many decades. Philosopher Karl Popper (1974), for example, was an influential proponent of antireductionism, characterising all phenomena into two types. 'Clock' phenomena, which have a mechanical basis and thus can be subjected to reductionism, and 'cloud' phenomena, which are indivisible and thus depend on emergence for explanation.

Emergence, as Van Regenmortel (2004) explains, is a way of dealing with the failures of reductionism by accounting for new features which are absent in the isolated components but which arise when the parts interact with each other and are influenced by their environment. Yet Popper argued that scientists "have to be reductionists" as "nothing is as great a success in science as a successful reduction" (1974: 259), given that such reductions provide a way of identifying the unknown with the known. Yet Popper also notes that such attempts at reductionism invariably fall short of achieving a complete reduction. As such he ultimately concludes that reductionism is more useful as a methodological tool (given that it is fruitful to science even when it fails), than as a philosophical one (Popper 1974).

However reductionism has not only served as a methodological and analytical tool within science. Rather, as Hayden notes, it has "long played a central role in debates about the power, folly, and violence of modern science" (2012: 272) (for further discussion see Haraway 1988; Shiva 1993; Stengers 2000). That is the violence of imposing reductionism in such a way that it dismisses other knowledges. As way of example Hayden notes that, in creating his 'universal' system of classification, Linneaus and his proponents were accused of "engaging in dangerously misguided substitutions and reductions of one kind of knowledge to another" (C. Hayden 2012: 272). Dismissing locally contextualised knowledge about plants and their effects, and thus "placing indigenous knowledges on the wrong side of truth itself" (C. Hayden 2012: 272). Thus, Hayden (2012) stresses that in 'going small,' reductionism aims to transcend the particularities of context, and in so doing, much knowledge and information is obscured and discarded.

A typology of reductionism and antireductionism

In addressing the conceptual critique of reductionism, Nagel (1998) identifies a typology of reductionist and antireductionist positions. Constitutive reductionism, Nagel (1998) claims, holds that everything is made of the same elements, while explanatory reductionism maintains that the laws governing those elements can be used as an ultimate explanation for everything that happens. In response, epistemological antireductionism holds that even if 'in reality' everything can be explained using particle physics, we are unable to grasp such 'ultimate' explanations for most complex phenomena. Thus we must make do with simplified explanations. Nagel (1998) contends that such epistemological antireductionism is compatible with constitutive reductionism and is thus largely uncontroversial. Ontological antireductionism, however, addressing as it does what the world 'really' consists of, instead of our knowledge of the world, is rather more controversial.

Nagel (1998) argues that there are two forms of ontological antireductionism, explanatory and constitutive. Explanatory ontological antireductionism holds that, ontologically, there are physical phenomena for which an explanation at the most basic, universal level is inadequate. For those who adopt this form of ontological antireductionism it forms the basis of an argument for emergence (Nagel 1998) and thus links back to Popper's notion of cloud phenomena. The other, more controversial form of ontological antireductionism addressed by Nagel (1998) is constitutive ontological antireductionism, and includes the notions of vitalism and holism.

While both vitalism and holism oppose mechanism, maintaining that the whole is greater than the sum of its parts, the main difference between these two concepts is metaphysical. Vitalism can broadly be defined as the notion that "living organisms are fundamentally different from non-living entities because they contain some non-physical element or are governed by different principles than are inanimate things" (Bechtel and Richardson 1998). This non-physical element is often referred to as the *Élan vital*, a term coined by Henri Bergson (1911) and translated as either the vital impetus (Papanicolaou and Gunter 1987) or the vital force (Brooks 2001). While traditional vitalism, that which espouses the existence of a vital force (Bechtel and Richardson 1998; Mayr 2002), is now widely considered redundant, reductionism remains unable to completely quell its opposition. As Morange (2008) discusses, although the advances of molecular biology led many to believe that the question of 'what is life?' had been answered, in recent years scientists have become increasingly convinced that we do not in fact have the complete answer. While Morange (2008) asserts that this does not necessitate a resurgence of vitalism's spiritualism, Canguilhem (2009) and Greco (2005), for example, follow in Bergson's (1911) own footprints by arguing that, although the notion of an *Élan vital* may not explain much scientifically, it still serves as a resistance to reductionism by highlighting our ignorance when it comes to life.

The notion of holism however, a term coined by Jan Smuts (1926), describes an approach to understanding the world which Smuts argued had no need for the explanatory powers of an *Élan vital*. Smuts instead contended that the synthesis of parts to make a 'whole' "affects and determines the parts, so that they function towards the 'whole'; and the whole and the parts therefore reciprocally influence and determine each other" (1926: 88) in such a way that they cannot be independently understood. Many, including Fodor and Lepore (1992), Bischof (1998), Jackson (2003), and Laszlo (2002, 2004) have subsequently followed in Smuts' footsteps to critique reductionism by suggesting the need for a holistic approach to understanding our world. Yet despite not invoking the notion of an *Élan vital*, Human (2015) argues that holism often leads to some form of mysticism. This, he asserts, is due to the difficulty of answering the question of what exactly the whole *is* and how we can deal with such a high degree of complexity (Human 2015).

As is clear from the above discussion of reductionism and antireductionism the subject is fraught with philosophical debate. While I am interested in this discussion, it is not the focus of this thesis. Synthetic biology with its goal of rendering life as engineerable material is an, if not, 'the,' exemplar of reductionism. Yet it is not the merits or accuracy of reductionism per se which

I am addressing here. Rather, I am interested in exploring synthetic biology as a case study to examine the issues, both practical and conceptual, which arise when synthetic biologists attempt to enact their reductionistic approach to biology.

Reductionism in synthetic biology

In 1966 Francis Crick gave a series of lectures at the University of Washington in which he discussed vitalism and the nature of life. During these lectures he noted that a way to refute vitalism would be to create a living organism synthetically, something which synthetic biology is actively striving to achieve. Indeed, Crick's book *Of Molecules and Men*, opens with the quote "Exact knowledge is the enemy of vitalism" (1966). Thus Crick noted that, "[i]t seems to me far more important to be able to understand a living cell . . . than to worry about whether we could synthesize it completely, starting from the elements" (1966: 64). Such knowledge, of the structure, function, and control mechanisms of a living cell, Crick maintained, would spell the end of vitalism and thus the ultimate success of reductionism. However, as Popper addressed in 1974, and as Rose acknowledged in 2013, such knowledge of life still eludes us. For Popper this lack of understanding was partly responsible for his conclusion that the philosophy of reductionism was a failure. He argued that even if we manage to produce life from inanimate matter it would not amount to a complete reduction if we do not fully understand what we are doing.

In the intervening years, with the production of the likes of Dolly the sheep and Synthia, the so-called 'first synthetic organism,' it would seem that life has indeed become amenable to intervention and control (N. Rose 2013). As Morange explains, the reduction of life to physicochemical phenomena has had the consequence of "favouring research into the use of organisms for commercial purposes." Thus, "[i]t is not by accident that the development of this field, biotechnology, should have coincided with the growing domination of a reductionist conception of life" (Morange 2008: 8). Yet Rose is quick to point out that while the "fantasies of omnipotence" that underlie this shift towards biotechnology "inspire much utopian and dystopian speculation," they also "grossly overestimate both our knowledge and our technical capacities" (N. Rose 2013: 6).

Synthetic biology's practical and conceptual challenge: how to render biology engineerable?

Addressing the reductionistic vision of synthetic biology, itself part of the shift towards biotechnology that Morange (2008) addresses, Rose (2013) notes that the fantasy of being able to remove bio-parts from their origins and functionally link them together, in order to synthesise a living cell from its elements, is misleading. There is, after all, still so much that we do not know. Thus it would seem that synthetic biology is doing exactly what Crick advised against. It is attempting to synthesise life completely from its elements without first acquiring a full understanding of its structure and workings.[28] While any success would be, by Popper's reckoning, an incomplete application of reductionism, more importantly, for my purposes, trying to apply its stringent version of reductionism without this full understanding submerges synthetic biology within a quagmire of practical and conceptual challenges. Ultimately then, it is these challenges, which the synthetic biologists at the Centre have to navigate, and that I address within the following chapters.

Synthetic biology is, as mentioned above, an emerging hybrid discipline, which is posing the question, how can one apply an engineering approach to biology, and therefore life? As discussed above, addressing this question raises both practical and conceptual issues. Thus examining it requires a focus on both the disciplines' practical and conceptual norms. As such, where chapter four addresses the practical day-to-day work of synthetic biologists attempting to apply an engineering approach to biology, and thus establish an epistemic culture for the discipline, chapter five examines how these same synthetic

[28] Indeed, even the simplest, synthetic organism defies complete understanding. In 2016 Craig Venter and his team announced their creation of the smallest, simplest self-replicating organism, syn3.0 (Clyde A. Hutchison et al. 2016). The authors note that their goal was to produce "a cell so simple that we can determine the molecular and biological function of every gene" (Clyde A. Hutchison et al. 2016: 1414). Yet, of syn3.0's 473 genes, genes that are deemed essential to the organism remaining alive, its creators admit that they do not understand the biological function of 149 of them.

biologists conceptualise the products of that work. In this way chapter five addresses my third research question by asking whether the synthetic biologists at the Centre see their 'products' as machines, as organisms, or as hybrid entities that blur the boundary between the two? Drawing on a range of more conceptual literature (e.g. Arthur 2009; Canguilhem 2009; Deplazes and Huppenbauer 2009; Haraway 1997; Keller 2002; Latour 1987; Woese 2004) chapter five thus taps into the reductionism debate discussed above by addressing how the synthetic biologists at the Centre approach the age-old question 'what is life?' as well as the analogous, but less controversial, 'what is a machine?'

Keller writes that "the question 'what is life?' is a historical question, answerable only in terms of the categories by which we as human actors choose to abide, the differences that we as human actors choose to honor, and not in either logical, scientific, or technical terms. It is in this sense that the category of life is a human rather than a natural kind" (2002: 294). I argue in chapter five that a similar argument could be made regarding the question 'what is a machine?' As such, instead of engaging in the accuracy of synthetic biology's reductionistic claims, by examining whether the 'products' of synthetic biology are 'really' machines or organisms, I focus instead on the conceptual categories the synthetic biologists are creating, and the differences they are honouring, in regards to synthetic biology's 'products.' Exploring the ways in which the synthetic biologists at the Centre make sense of their products therefore, provides an interesting insight into, what Rose (2007) would term, their philosophy of life.

However the roots of synthetic biology's reductionism, that which has led the discipline to this point, are examined in chapter six. Indeed chapter six explores the fourth of my research questions by asking how synthetic biology fits into the broader history of attempts to investigate and shape the biological world? As detailed in chapter six, scientists and engineers have long attempted to artificially create life, create artificial life, and understand biology through mathematical models and similarities with physical and mechanical processes and devices. Chapter six thus draws on this rich historical literature in an attempt to explore synthetic biology's diverse heritage and to investigate whether this emergent hybrid discipline can be thought of as part of a wider attempt to both 'do' and think of biology differently.

In exploring whether synthetic biology is part of a potential conceptual shift within biology, I draw on a wide range of contemporary and historical literature looking at previous shifts in the conception of biology dating back to Aristotle's time. Exploring Canguilhem's (2000) conceptual chain of, life as animation, life as mechanism, life as organisation, and life as information, chapter six explores the gradual creep of reductionism and mechanism into our understanding of life throughout these conceptual shifts. Chapter six then explores how this embrace of reductionism and mechanism has brought us to a point of convergence between biology and engineering whereby the most recent of Canguilhem's conceptions of life, life as information, is arguably being replaced by that of life as engineerable material.

Finally, Chapter seven serves as a conclusion. Placing synthetic biology in the historical context discussed in chapter six, chapter seven reiterates that this emerging discipline is, in a significant sense, a response to, and an echo of, previous approaches to both doing and thinking about biology. Yet synthetic biology is, ultimately, a project to control life at the molecular level. In taking this approach to biology and life, synthetic biology is, as detailed in chapter six, embracing the reductionism and interventionism common amongst others who have attempted to engineer life. However, synthetic biology appears to be taking its brand of interventionalist biology to a new extreme, one that may prove to be part of a wider conceptual shift within biology towards seeing life as engineerable material. Nevertheless, despite their embrace of reductionism and mechanism, as chapter seven highlights, there is much about life and biology that still defies understanding and control. Furthermore, despite claims that synthetic biology is the uncomplicated hybrid of engineering and biology, which is unproblematically applying an engineering approach to biology, as highlighted in chapters three, four, and five, there is, ultimately, a lot more going on 'under the hood' as it were.

Yet, despite the obstacles and tensions addressed in the previous chapters, chapter seven highlights the ways in which the concerted efforts of synthetic biologists to see life in these terms influences the ways in which they speak about, think about, and practice biology. As well as their understandings of the 'products' of their work, and thus their categorisations and interpretations of 'life', 'organisms,' and 'machines.' Ultimately then, chapter seven draws the two halves of this case study's story together. The work being done to establish a discipline with the expressed goal of engineering, and thus controlling, life at the molecular level, and the work being down to bring this goal to fruition.

Chapter Two: Methodology

Science has been studied 'in practice' since the late 1970s and early 1980s. A time when the first laboratory ethnographies were undertaken by the likes of Latour and Woolgar (1979), Knorr (1981), and Lynch (1985). Hess refers to such works as "the first generation of STS[29] ethnographies," a generation which challenged the "naïve view of scientific work as a purely rational process of representing a nature that revealed itself in transparent observations" (Hess 2001: 234). Through utilising ethnographic methodology, these ethnographers investigated science and technology through direct observation and discourse analysis, focusing their attention on "the root of where knowledge is produced, in modern science typically the scientific laboratory" (Knorr Cetina 1995: 140). As Karin Knorr Cetina addresses, this generation of STS ethnographies were influential in, and influenced by, the rise of constructivism in STS, a theory which "holds reality not to be given but constructed" (1995: 147). Thus these early laboratory ethnographers worked to uncover the everyday, mundane processes of knowledge production in science. Processes that, arguably, lead to scientific findings being black-boxed as 'objective' facts and 'given' entities (Knorr Cetina 1995).

With time, this first generation of STS ethnographies was followed by a second generation and with this generational shift came a broader focus. According to Hess, second generation STS ethnographies tended "to be more oriented toward social problems (environment, class, race, sex, sexuality, and colonial) in addition to theoretical problems in the sociology and philosophy of knowledge" (2001: 236). Moving outside of the laboratory and away from expert knowledge, the second generation of STS ethnographies have, Hess argues, taken a multi-sited approach to look at the likes of activists, lay groups and the media. Relying more and more on documentary sources and

[29] STS variably stands for Science, Technology, and Society, or Science and Technology Studies, both of which denote the social scientific study of science and technology in their social context.

interviews and less on fieldwork in order to explore the "contours of orthodoxy and heterodoxy in a discipline's development" (2001: 236).

Yet, despite their differences in focus and approach, the combined efforts of these two generations of ethnographies have clearly shown science to be a social practice (see for example: Forsythe 2001; Gusterson 1996; Knorr Cetina 1999; Latour and Woolgar 1979; Martin 1995; Rabinow 1996, 1999; Traweek 1988). Thus, in my efforts to study the social dynamics of synthetic biology in practice I have drawn theoretical and practical assistance from across both of these 'generations' of work.

Like the first generation ethnographies my research relied heavily on fieldwork and was focused within the laboratory, and while it is multi-sited like the second generation ethnographies, like the first it is scientists themselves, rather than other interested parties, that are the participants. Yet unlike the first generation I have not focused exclusively on scientific knowledge or on unpacking any particular fact claim. Rather, I am interested in how synthetic biologists' attempts to 'engineer biology' shape both their day-to-day work and the way 'biology' and 'the biological' are consequently understood and interacted with within this emergent hybrid discipline. My lens for exploring these questions was the, then newly established, academic synthetic biology research centre located within a prestigious UK university, which was discussed in chapter one, and which I refer to as 'the Centre.' Thus, as Woolgar (1982) urged ethnographers of science to do, I undertook a study *in* a laboratory, not *of* a laboratory, focusing on questions with broader relevance than just the day-to-day work of the laboratory itself.

Entering the field

In November 2009 I began making contact with people at the Centre via email. I contacted Sara, the person in charge of the Centre's laboratory meeting series, and Peter, the lecturer in charge of the Centre's undergraduate synthetic biology course, to see if I could sit in on both. While Sara and Peter were both seemingly puzzled by my requests, and uncertain of my motivations, they thankfully consented. I had to wait until February for the course to begin, but by December I had begun attending the Centre's weekly, alternating laboratory and journal club meetings. This proved to be a good way of easing myself into the 'field' and starting to get to know more about the Centre and those who worked within it. My first attendance at a laboratory meeting was, as I noted in my fieldnotes, rather awkward. I had arrived at the University with ten minutes to spare, carrying a map of the campus, with the biochemistry building circled in yellow highlighter, my notebook and several back-up pens. After winding my way through the maze of buildings I found the Biochemistry Department and climbed its front steps. The glass sliding doors opened into a reception area containing a large security desk flanked by swipe card-activated gates, which stopped me in my tracks. I had no choice but to approach the security guard and ask him to let me through. However, rather than admit me to the building he telephoned Sara to tell her I had arrived and asked her to come and fetch me. Five minutes later Sara, a blond haired, bespectacled woman, who appeared to be slight annoyed by the inconvenience, came down the stairs to greet me and I followed her back up to the sixth floor doing my very best to make small talk and feeling every bit the untrusted, bothersome outsider.

We finally arrived at the sixth floor landing and went through a swipe card activated security door into a narrow hallway before veering off into a small, windowless room containing a large table, too many chairs, and a white board. The room was empty, but people soon started to arrive. I began to feel increasingly awkward as each new person assessed me with querying looks but did not actually speak to me. I decided to introduce myself to people, and tried hard to engage them in small talk, but not one of them would commit to a conversation. Malcolm, one of the Centre's directors, finally arrived and actually asked me a question "*Are you from LSE*[30]*?,*" but he responds to my affirmation with nothing more than a simple nod. To my great relief the meeting finally commenced, taking the silent focus off the lone social scientist in the room.

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30 London School of Economics and Political Science.

After my initial attempts at conversation I spoke very little during this first meeting as, despite racking my brain, I could think of no intelligent-sounding questions to ask, or comments to make. On bidding everyone farewell, and having received permission to continue attending the meetings, I was determined to do two things; one, drag the knowledge obtained through my own degree in Biochemistry back into the light, and two, build trust and rapport with the inhabitants of the Centre, my 'subjects', even if it required my attendance at many more meetings before they spoke to me.

At this time I also began attending various meetings and conferences of the wider synthetic biology community. In 2007 the Engineering and Physical Sciences Research Council, the Biotechnology and Biological Sciences Research Council, the Arts and Humanities Research Council, and the Economic and Social Research Council jointly funded seven synthetic biology networks across the UK. The purpose of these networks was "to develop and establish communication and networking between researchers in the biosciences, engineering and the physical sciences in the area of synthetic biology, with associated input from the social sciences and humanities" (Biotechnology and Biological Sciences Research Council). It was hoped that the networks would help to break down disciplinary language barriers and build an interdisciplinary synthetic biology community in the UK through which new research partnerships could be formed.

To this ends, the networks each organised annual one and two-day meetings of their members and other interested parties. In order to explore the interactions between engineers and biologists, as well as the conception of biology evident within the broader synthetic biology community, I attended five of these meetings during 2010. During 2009 and 2010 I also attended several synthetic biology public engagement events, to witness how synthetic biology was being presented in this context, and two synthetic biology symposia held at the Centre for the wider disciplinary community. In June 2011 I attended, and presented a poster at SB5.0, the most prominent international synthetic biology conference series, which was held at Stanford University, California. This conference, like those in the UK, proved an interesting forum for exploring the conceptions of biology within the broader synthetic biology community and the relationship between biology and engineering as it was being presented.

Yet all of these activities served to supplement my main research activity, an ethnographic study of the day-to-day practice of synthetic biology within a newly formed research centre. My aim at the beginning of my fieldwork was to explore the interactions between biology and engineering, and thus biologists and engineers, working within the Centre. I intended to focus on their attempts to embrace the engineering approach to biology, central to synthetic biology's aim, and to explore the ways in which 'the biological' and 'the engineered' were being constructed, understood, and interacted with within the Centre. However when I began my fieldwork the Centre itself was more conceptual than it was concrete. Its members were scattered throughout the University or, having recently been hired, still resident at other universities. Indeed, it was not until April 2010 that the Centre finally moved into its long awaited office and lab space within the Engineering School, and thus became more of a tangible reality.

I had been promised space within the Centre to work, and I knew my ethnographic research would benefit from more continual contact with the synthetic biologists, so I was eager to 'move in.' I hoped to take on the tasks of a laboratory assistant, as Latour (1979) had for *Laboratory Life*, in order to participate in the workings of the Centre as fully as possible. Such participation, which is central to ethnographic research, would, I reasoned, aid my understanding of the synthetic biologists' behaviour and thoughts. As Emerson et al. claim, through "participating as fully and humanly as possible in another way of life, the ethnographer learns what is required to become a member of that world, to experience events and meanings in ways that approximate members' experiences" (1995: 2). What I experienced and learnt while in the Centre shapes all that is to come in the following chapters. However before moving on to a discussion of these findings it is important, and hopefully interesting, to further describe and reflect on both my fieldwork site and my experience of and approach to this ethnography.

The Centre

My fieldnotes from my first visit to the new space, in May 2010, paint a picture of the Centre where I was to spend every weekday, and several evenings until mid-December. Sara had agreed to show me around the Centre's new space, and to help me find a desk to work at, so I met her in her office in the biochemistry department and together we walked across the university campus to a large, modern, glass building at the heart of the Engineering School. We entered through its wide sliding doors and crossed the foyer to the lifts. My newly acquired University ID card, proclaiming me to be a Visiting Researcher within the Division of Molecular Biosciences, had to be touched on the sensor pad within the lift before I could select a floor. This requirement, like the swipe card gates I had entered on attending my first lab meeting, served as a reminder of the security measures which bar all unaccompanied outsiders from accessing the university's laboratories. On exiting into the sixth floor lobby my attention was drawn to a set of locked double doors beneath a sign displaying the Centre's name. Using her own ID card, Sara swiped us through this threshold and started showing me around what would become the centre of my fieldwork world. To my eager eyes everything appeared shiny, new, and expectant. There were no scuffmarks on the floors, the walls were brilliantly white, and the labs and equipment immaculately clean.

Just inside and to the right of these first double doors was a glass wall with a door leading into the empty PhD office. The room was mainly white, with highlights of fuchsia pink, and a bright green door, a colour scheme that continued out into the corridor and throughout the Centre. The dark-grey, flecked carpet in the office blended into the hallway linoleum, which mimicked its shade and pattern. The room at the time contained four desks, two facing the sidewalls, and two facing the exterior glass wall of the building. However with time, and the expansion of the Centre, this number swelled to eight. Through this exterior wall, from the desk that would become my own, I could see down to the grey courtyard below and over to the roof of the adjacent building.

On returning to the hallway we were confronted by a second set of swipe card accessible swing doors leading through to the laboratories themselves. Four signs were prominently displayed on these doors each bearing an image surrounded by the iconic red circle with a line through it, indicating something forbidden, and the corresponding imperatives "No Smoking," "No Drinking," "No Eating," and "No gloves past this point." The image for this last one was the most unusual of the four, being a set of clasped hands in bright blue latex gloves.

Six rooms lay on the other side of these double doors, all of them unoccupied at the time. The first of which, to our left, was the 'prep room,' a small windowless room containing an array of chemicals, solution bottles, eppendorf tubes, and several electrophoresis machines for running gels. Directly opposite its open door was the first of the three laboratories with a handwritten sign on the door bearing the words "Johnson/Roberts lab," referring to Martin Johnson and Michael Roberts, two of the newly appointed synthetic biology lecturers. As with the PhD room, the hallway-facing walls of the three laboratories were made entirely of glass, so anyone in the hallway could observe the synthetic biologists inside as if they were part of a live action museum exhibit. Through the wall of this first lab I could see several clean bench tops, a tap that would become notorious for drenching anyone who turned it on, and two small PCR machines.

The other two laboratories were located on the opposite side of the hallway, past the prep room. The first of these laboratories housed the PhD students working with Alan Gregg and contained both 'the robot' and 'the FACS machine.' On being shown the FACS machine or, as my untrained ear heard it, the 'fax machine,' I was confused to see a contraption bearing a mechanical arm with a line of pipette tips suspended from it. It was, as I quickly learnt, a fluorescence-activated cell-sorting machine, while the robot was nowhere near as exciting as it had sounded, being a very large piece of nondescript apparatus sitting on the floor on the far side of the lab. Indeed it remained on the floor for several months, waiting patiently for the bench above to be extended and strengthened in order to accommodate it. Like the FACS machine, the robot was designed for the high-throughput work the synthetic biologists at the Centre were hoping to perform as they strived towards characterising and assembling synthetic biology 'parts.'

The third and final laboratory was introduced to me as 'Janet's lab,' referring to another of the synthetic biology lecturers, and the only woman above the level of PhD student actively working within the Centre. Like the other two laboratories, this one contained work benches, small freezers, shelves of supplies, camping gas stoves (due to a lack of piped-in gas in the Engineering School), coat racks hung with white lab coats, pipettes, boxes and boxes of different sized and coloured latex gloves, bright blue pipette tips, and eppendorf tubes. Centrifuges and mass spectrometers sat on bench tops, and sinks and rubbish bins with bags colour coded for different types of waste were by the doors – clear bags for waste that had been in contact with cells and therefore needed to be autoclaved[31] before disposal, and coloured bags for everything else. Opposite Janet's lab was a small room containing a series of incubators and freezers, and the 'hot desk' room, another small room containing three or four desks which was, at the time, being used by the undergraduate students doing their practical, small scale projects within the Centre.

Having shown me around these labs and offices, Sara then led me to the Centre's extra office space directly upstairs. The seventh floor area was a jumble of office furniture, with a maze of filing cabinets, desks, drawers, and shelves. Indeed way too much stuff for the size of the space, all of it waiting to find a home. There was a sink and a small fridge in one corner, just past a glass-walled, locked, and darkened office, which, Sara informed me, belonged to Michael and Janet. The glass wall into their office was scrawled all over with biological diagrams, and half thought-through reactions in what appeared to be a black whiteboard marker pen. There were no whiteboards up yet, so it

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[31] Sterilised with high-pressure steam.

seemed that someone had been making do with what was available. Against the left wall of the central open-plan area were two more glass-walled offices. Through the glass I could see Grant Butler (the fourth new lecturer) and Martin in the first, and said hello to them both. Sara mentioned to them that I would now be in the Centre fulltime, and to my great relief, they both reacted positively. The next office, which was still bare except for two empty desks, was apparently for the Centre's directors Alan and Malcolm, though at the time I was unconvinced that either would leave their respective department offices to take up residence in it. As it turned out my doubt was justifiable given that I never once saw either of them in there. We then headed back downstairs and, on saying goodbye to Sara, I headed back to LSE to gather up my belongings in order to take up residence at my new desk in the Centre the following day.

Life in the Centre

From my desk in the PhD room I had easy access to the laboratories, offices, and their inhabitants. During the eight months of my residence in the Centre I continued to attend the journal club discussions, laboratory meetings, Centre meetings, public symposiums and presentations, informal afternoon cake sessions (which I instigated), and networking and collaborative events for both the Centre and the wider UK synthetic biology community. However, between these engagements I spent my days shadowing the Centre's inhabitants as they worked in the laboratories or at their desks, providing assistance where I could, from loading and running electrophoresis gels and taking optical density readings, to helping to select diagrams for papers. Throughout my time in the Centre, and the various meetings and conferences I attended, I took detailed fieldnotes recording what I saw, experienced, heard, felt, and thought as I went about my days in the 'field.' These were either written into my fieldwork journal and later typed up, or they were typed directly into my laptop.

Writing fieldnotes, as Emerson et al. (1995) address, is central to any undertaking of participant observation. However "writing descriptive accounts of experiences and observations is not as straightforward and transparent a process as it might initially appear" (Emerson et al. 1995: 5) for there are many possible ways in which the same events and situations can be described. Thus Emerson et al. see fieldnotes as inscriptions of social life and discourse that transform "witnessed events, persons and places into words on paper" (Emerson et al. 1995: 9) which, depending on the person doing the inscribing, emphasise and exclude certain elements. As such, fieldnotes can be described as "written accounts that filter members' experiences and concerns through the person and perspectives of the ethnographer; fieldnotes provide the ethnographer's, not the members,' accounts of the latter's experiences, meanings, and concerns" (Emerson et al. 1995: 13).

Consequently my fieldnotes, which inform much of the substantive material in this thesis, must be seen as partial, ultimately representing my own account of the synthetic biologists' experiences and concerns rather than their own. The partiality of my fieldnotes is further increased by the fact that I did not take notes while I was 'in the field.' Being imbedded within my research site, the building of rapport with the synthetic biologists I was studying was essential. Therefore I avoided making 'open jottings' for my fieldnotes, as I believed that the practice of note taking during informal conversations, and Centre or laboratory activities, would have been distracting for the synthetic biologists and would have inhibited my ability to participate. So instead I took what Emerson et al. (1995) refer to as 'headnotes,' committing situations and conversations to memory so I could later write them down in my notebook or type them into my laptop when I returned to my desk.

Interviews

As Fontana and Frey (2000) acknowledge, participant observation and in-depth unstructured interviewing go hand-in-hand, as much of the data gathered during participant observation comes from informal conversations in the field. However, being aware of the partiality of my fieldnotes led me to also undertake in-depth semi-structured interviews with the Centre's inhabitants. Towards the end of my time in the Centre I contacted all of its immediate members, and several associated members, via email or in person and asked them to participate. Of the twenty-four individuals I identified as potential interviewees, twenty-two agreed to be interviewed. The other two, who were associates of the Centre, did not respond despite multiple attempts to contact them. Written consent was obtained prior to each of the interviews, which were undertaken in private and lasted between forty-five minutes and two hours. Preliminary analysis of the themes emerging from my fieldwork helped to shape the questions I used for the interviews, allowing me to further explore, and challenge, these themes. I took a semi-structured approach to these interviews as I wished to avoid both the rigidity of structured interviews and the free-form approach of unstructured interviews, having already utilised the latter during my participant observation. I audiotaped each of the interviews and sent the digital files to a professional stenographer to transcribe. In order to maintain the interviewees' anonymity I ascribed each a number, which was attached to both the audio file and the transcript of their interview. The twenty-two interview transcripts I received back from the stenographer, and all of my detailed fieldnotes, were uploaded into NVivo8 where I coded them for emergent themes, first broadly and then more finely. These themes are explored in the following substantive chapters.

Although I undertook these interviews as a way of both uncovering more in-depth information than I was able to elucidate through the participant observation, and giving those at the Centre a chance to reflect on the practices I was observing, I was undoubtedly also an active participant in the interviews, helping to shape the information I received. As Fontana and Frey write "[i]nterviewers are increasingly seen as active participants in interactions with respondents, and interviews are seen as negotiated accomplishments of both interviewers and respondents that are shaped by the contexts and situations in which they take place" (Fontana and Frey 2000: 663). Thus although I wished to hear the synthetic biologists' own accounts of how they understood and experienced the work they do, it must be conceded that "*what* the ethnographer finds out is inherently connected with *how* she finds it out" (Emerson et al. 1995: 11). Consequently, not only did I shape what I found out through the questions I asked but also, as the interviews were transcribed from audio files into transcripts, and it was these transcripts that I analysed, certain dimensions of meaning were lost. Through the exclusion of emphasis, silences, incomprehensible words, and overlapping speech, transcripts lose nonverbal cues to meaning which aid in the understanding of discourse (Emerson et al. 1995).

Embracing subjectivity and reflexivity

Barnard writes that "[i]t is impossible to engage in ethnography without some idea of what is important and what is not" (Barnard 2000: 4-5). A comment that is distinctly different from, and to my mind more accurate than, Oakley's (2000) claim that, "[i]t is generally true that what people look for they will find, and that what they are not looking for will probably escape them" (Oakley 2000: 52). For, while my interview questions undoubtedly affected what I found, and I indeed only recorded certain things during my participant observation, I dispute that this led me to only find what I set out to find. I entered the field with what Bronislaw Malinowski, arguably the father of participant observation, would call 'foreshadowing problems.' That is, problems or topics of interest, which, as he argues, is not the same as having preconceived conclusions. On this Malinowski wrote:

> "[g]ood training in theory, and acquaintance with its latest results, is not identical with being burdened with 'preconceived ideas.' If a man set out on an expedition, determined to prove certain hypotheses, if he is incapable of changing his views constantly and casting them off ungrudgingly under the pressure of evidence, needless to say his work will be worthless. But the more problems he brings with him into the field, the more he is in the habit of moulding his theories according to fact, and of seeing facts in their bearing upon theory, the better he is equipped for the work. Preconceived ideas are pernicious in any scientific work, but foreshadowed problems are the main endowment of a scientific

> thinker, and these problems are first revealed to the observer by his theoretical studies" (1922: 7).

This need, for ethnographers to remain open to the unexpected, is also highlighted by Hammersley and Wilkinson who write that, for ethnographers "their orientation is an exploratory one" (2007: 3). Thus, they continue, "[i]t is expected that the initial interests and questions that motivated the research will be refined, and perhaps even transformed, over the course of the research; and that this may take a considerable amount of time" (Hammersley and Wilkinson 2007: 3). As my own research progressed, new, unanticipated avenues of investigation opened up as I learnt and experienced more of synthetic biology at the Centre. Thus these unexpected findings in turn altered and refined my initial research questions and interests much as Malinowski, and Hammersley and Wilkinson, describe.

Oakley's (2000) questioning of the trustworthiness of qualitative research however goes further. She claims that as the findings of qualitative research are uncontrolled and cannot be reproduced and repeated, they are untrustworthy; unreliable that is rather than false. Oakley asserts that researchers cannot shed the power of being the researcher and interpreter of their findings, that is "the power to define" (Oakley 2000: 72), and thus the work they produce is not inherently a reliable account. Denzin and Lincoln also acknowledge this predicament in relation to research observations, writing, "[t]here are no objective observations, only observations socially situated in the worlds of – and between the observer and the observed" (2005: 19). Thus given the inherent subjectivity of such research, it is important for researchers to embrace reflexivity. Regarding reflexivity, Hammersley and Wilkinson write:

> "[t]he concept of reflexivity acknowledges that the orientations of researchers will be shaped by their socio-historical locations, including the values and interests that these locations confer upon them. What this represents is a rejection of the idea that social research is, or can be, carried out in some autonomous realm that is

> insulated from the wider society and from the biography of the researcher, in such a way that its findings can be unaffected by social processes and personal characteristics" (Hammersley and Wilkinson 2007: 15).

Nevertheless, this subjectivity, and the recognition that research is an active process of observation, interpretation, and writing, does not, and should not, devalue the findings of qualitative social research. As Hammersley and Wilkinson write, "to say that our findings, and even our data, are constructed does not automatically imply that they do not or cannot represent social phenomena" (Hammersley and Wilkinson 2007: 16).

In the interests of reflexivity then, it is important to address elements of my own biography that have had a significant effect on the findings of this research, both in terms of the way I interpreted my observations and findings and in terms of how my presence in the Centre altered what went on. As an undergraduate student my interest in science generally, and in the workings of biology specifically, drew me to university studies in biochemistry and later (when courses became available) in genetics. However, as I also had a keen interest in learning about the social world, I simultaneously undertook a degree in anthropology. Following the completion of my BSc and BA I embarked on two further research degrees in Anthropology, an Honour's and a Master's degree, both of which explored social aspects of medicine and science through the use of ethnography. Following the completion of my Master's degree I undertook three separate academic research jobs in ethnographic projects, one in my native New Zealand and two in the UK, which likewise explored the social aspects of science and medicine. It was from this hybrid academic background that I embarked upon my doctoral research on synthetic biology.

Synthetic biology was a subject that interested me both for the advances in science it promised and for the social and scientific implications that come with such advances, or attempts at such advances. My academic experience, alongside my knowledge of science and of biology in particular, undoubtedly shaped the way I interpreted what I saw and experienced during my fieldwork. The Centre, and its laboratories, while a new environment for me, were not foreign and strange in the way Latour and Woolgar describe (1979). Nor was their scientific language completely alien to my ear, as it would perhaps have been for an ethnographer with no training in science. Throughout the project I have drawn heavily on my knowledge and experience of biology to understand the science utilised and produced within synthetic biology and to help build rapport with the synthetic biologists. My science background, for example, appeared to reduce some of the synthetic biologists' suspicions of me and my research. Indeed, on more than one occasion I was introduced to visitors to the Centre, by Malcolm Brown,[32] as "*our resident social scientist, but really she's a biologist.*"

I further utilised my familiarity and experience within biological laboratories to help those I shadowed with their experiments, adopting the role of a lab assistant, much as Bruno Latour did in *Laboratory Life* (Latour and Woolgar 1979). This helped me to fulfil both the 'participant' half of my participant observation, and my desire for reciprocity. Nevertheless it would be naïve to believe that the inhabitants of the Centre did not see me as 'other.' I was clearly an anomaly in the Centre, being the only resident social scientist, and at times they were visibly perplexed by my research methods and interests. Furthermore, due to the impetus within synthetic biology (largely due to the requirements of funders) to address Ethical, Legal, and Social Issues (ELSIs), the inhabitants, familiar with the rhetoric which was expected of them, may have told me what they thought I wanted to hear.

My knowledge of science was, however, at times a hindrance. I arguably did not look on the field of synthetic biology with the same 'fresh eyes' that I would have if I had never studied biology, so I may well have overlooked aspects of their practice that would have interested other ethnographers. Furthermore, knowing I had a degree in Biochemistry, the synthetic biologists at the Centre would often over-estimate my familiarity with the concepts and

[32] The Centre's director with a background in biology.

procedures utilised within synthetic biology; assuming that I understood what was going on, or what they were saying, when sometimes I did not. This either led to me requesting that they repeat or explain things to me again (feeling all the time like I should not require the explanation), or to me remaining in the dark rueing that my biological knowledge had grown rusty. If I had no background in biology at all, the synthetic biologists may have been better primed to explain things to me, and I may have felt less self-conscious about asking. Or it is equally possibly that I may simply have suffered in the dark more often. Or indeed I may have experienced both.

These feelings, that I wasn't collecting all the data I could, or should be, and others such as the fear that I had 'found nothing' or that I wasn't doing enough, that I was missing things, are common amongst ethnographers as they embrace the position Hammersley and Wilkinson refer to as being a 'marginal native.' This insider/outside role sees ethnographers "intellectually poised between familiarity and strangeness" (Hammersley and Wilkinson 2007: 89) as they endeavour to maintain some social and intellectual distance from the group they study. Negotiating this marginal role can be particularly difficult when you cannot escape 'the field.' As such I was grateful that my research site was located in the city in which I lived, so I could exit 'the field' and return home each evening, and also in the same city as my 'home' research centre. The ability to leave the company of the synthetic biologists and reconnect with a group of social scientists arguably enabled me to maintain some distance from my research participants, as my social science colleagues would help me to question and challenge my findings as they emerged.

Access and power

Access to 'the field' is frequently tricky to negotiate for the ethnographer. However in this respect I was incredibly lucky. My 'home' research group BIOS at the LSE, had formed a partnership with the Centre for the purposes of applying for an EPSRC grant on synthetic biology. The grant required the successful applicants to include an element of social science research within their programme of work, and thus the joint application included the provision of a PhD studentship for a social scientist. As luck would have it, I was granted that studentship. While this position undoubtedly helped me to gain access to the synthetic biologists and the Centre itself, my role within my fieldwork site was not straightforward. I was, like many ethnographers, both an insider and an outsider in my fieldwork site, a position that often left me feeling I was simultaneously a member of the Centre, and an interloper.

For example, after several months of attending laboratory meetings I was asked to lead a laboratory meeting myself and present my own work. This was a daunting prospect, as the language, methods, and approaches of social science were foreign to most in the room, and gaining their good opinion felt crucial at that stage in my research. I was still building rapport with the members of the Centre, and I hoped that I would get their approval to undertake a more in-depth ethnography with them. To my great relief my presentation, on the history of attempts to apply an engineering approach to biology, seemed to go down well. However, as well as some interesting and gentle questions from those in the audience I also received a couple of questions and comments from Malcolm Brown, which were rather loaded. First he asked me about the point of social science research. Is it, he queried, "*just for fun*" or does it actually have a wider (and, by implication, more worthwhile) purpose? Later on, when the discussion turned to the recent hassles over acquiring equipment for the Centre's new space, he turned to me and said "*see what we have to deal with, you just have to hope the internet connection is working*". He then followed this comment with, "*it must be nice just having to sit at a desk and read.*"

While all of these comments were said in a friendly, joking tone, he made it very clear that he thought we social scientists have it easy and that we don't produce anything of real use. One of the newly hired lecturers, Martin, did at this point jump to my defence saying, in reference to a BMJ paper I had quoted, "*she is digging up papers from 1910!*" to which Malcolm replied, "*yes, I'm sure it's not as easy as it seems.*" Thus while I was ostensibly welcome within the Centre, at least some of its members, and most prominently

Malcolm, were sceptical of my research. Over the twelve months that I was a constant presence within the Centre there were several such occasions where I found myself needing to explain social science, or having to listen while social scientists and social science were openly, albeit good naturedly, mocked. However despite this, I was always treated well by the members of the Centre, helped in part as discussed above, by my own background in science.

Nevertheless, given the nature of the partnership between BIOS and the Centre, I was not simply viewed as an independent researcher who was spending time in the Centre, but rather I was seen as a member of the collaboration with a role to play. Thus on several other occasions Malcolm and Alan, as directors of the Centre, attempted to make use of me as a spokesperson for the Centre's commitment to 'ELSI,' to convince visitors that the Centre was taking such issues seriously and was actively engaging with them. This was always an awkward situation, as I felt torn between being a compliant and helpful insider/member of the Centre on the one hand, and being honest about the shortfall of their engagement with ELSI as an outsider/ethnographer on the other. It also seemed at times that the directors believed my mere presence within the Centre was all the evidence necessary to fulfil the social science requirement of their funders. Thus, despite being informed about the nature of my research on multiple occasions and giving their approval for it, Malcolm and Alan did not always seem to recognise the potential output of ethnographic fieldwork. To this ends, Malcolm joked on several occasions that there should be a formal agreement that the social scientists working with them would not "*write a book about them like Rabinow and Bennett did!*" referring to the book Paul Rabinow and Gaymon Bennett wrote about their own collaboration and ethnographic interactions with synthetic biologists (Rabinow and Bennett 2012).

As one desired outcome of my own ethnographic fieldwork is published work, which will logically be based around findings from my fieldwork in the Centre, this 'joke' was decidedly unsettling. Given the nature and location of my fieldwork I could almost guarantee that anything I did publish would be read by at least one person within the Centre, and this came with a concern that, should they disagree with what I had written, or feel uncomfortably exposed by it despite my commitment to maintaining their anonymity, I could jeopardise my future access to the field, not to mention their friendship.

This situation is indicative of a shift in the power dynamic between the ethnographer and her informants. For unlike traditional ethnographies where the ethnographers would retreat from their fieldwork sites to write up and publish their work in locations and languages frequently foreign to their informants, in ethnographies of science, as in other contemporary ethnographies, the informants are likely to carefully read what the ethnographer studying them has written (Forsythe 2001; Hess 2001). While this more equal distribution of power is welcome within ethnography, it does place ethnographers in a more challenging position. One where their informants may attempt to sensor their work, or bar their access to future research should they dislike what they read (Forsythe 1999).

Hess (2001) notes that a further challenge of ethnographies of science is that their fieldwork site(s) are often part of a rapidly changing and emerging world, thus both the ethnographer and the informants are trying to figure out what is happening. This was most certainly the case for my informants, my research site, and me, for neither the Centre nor for that matter the discipline of synthetic biology, seemed fully formed at the time of my fieldwork. As such, the ethnographic findings that follow are, perhaps more so than most, tied to a certain time and place. They capture my own ethnographic understandings of the field of synthetic biology, the Centre I studied, and the individuals who worked there, as they were in 2009-2010. Things have, as one might expect, moved on and changed in the interim. However as the Centre was the first academic synthetic biology research centre in the UK, and was touted at the time of my fieldwork as the most important site for synthetic biology in Europe, I believe that the site itself maintains its significance. Furthermore, as I was interested in studying the emergence of this discipline and the ways in which people, ideas, and approaches from different disciplines came together within it, I maintain that the findings of this ethnography are significant and important, even if, and perhaps especially if, the discipline has subsequently matured and become less messy.

Exiting the field

Having spent twelve-months actively trying to build rapport and trust with the members of the Centre, I had developed friendships and working relationships with many of the people there. As such the attitude of the Centre's members towards me had shifted a long way since that first awkward meeting where they viewed me with suspicion. I was part of the Centre now, admittedly an idiosyncratic part, but a part nonetheless. I had been a member of the team of advisors for the iGEM[33] team, I had presented my work at lab meetings like everyone else, they were used to seeing me in a lab coat, and we had talked through our work with each other.

Members of the Centre would share titbits of gossip and information from meetings with me that they thought I would find interesting. And I had become the 'go to' person for any questions about 'the public,' ethics (despite stressing countless times that I was not an ethicist), and how to make their work more socially acceptable. While I did not always feel comfortable with these questions, being the person to speak to about them gave me a role within the Centre alongside that of the general 'dogs-body' who could be relied upon to willingly perform tedious tasks such as labelling eppendorf tubes. Both roles gave me a sense that I was delivering a degree of reciprocity, especially when, after a chat about whether synthetic biology was playing a role in changing the focus of biology, David said "*it's good to think about things other than our research and you make us do that*." Thus exiting from the field was always going to be difficult.

I did however have a very good excuse to retreat from the workplace; I was pregnant and about to go on maternity leave. I therefore thought I had avoided the awkwardness of exiting the field, but it turned out that I had just delayed it. I received many emails from members of the Centre asking me

[33] International Genetically Modified Machine's competition.

when I would return, and assuring me that Hayden, who had taken over my desk, could be made to shift. While it was flattering to hear that they wanted me back, it also meant that I had to explain that I was not coming back, at least not permanently. I would attend the occasional meeting, and pop by when I needed to clarify something, or ask further questions, but I was not moving back in. On one of my first days of fieldwork Grant had joked, as I explained ethnography to him, "*so, we'll be your E. Coli?*" but with time and effort the fact that I was studying them had stopped overshadowing our interactions and they had relaxed. Sadly however, on exiting the field, and thus leaving the Centre, it felt as if the fact that I had been 'studying them' had been brought back into the spotlight.

Chapter Three: Negotiating an Epistemic Cultural Divide

The lab meeting began like any other. People filtered in and found themselves a seat at the table if they were early enough, or against the back wall if they weren't. Once everyone had arrived the general chatter stopped and we sat, cramped into the same tiny, windowless room where I had first encountered most of the members of the Centre. Everyone listened attentively to Christian[34] talk about his work on *in vitro E. coli* cell-free transcription and translation systems, which he referred to as a "*a new 'chassis', if we carry on with the synthetic biology language*."[35] Christian's talk outlined his interest in developing a cell-free chassis that can be used in biosensors, specifically a biosensor that can detect the pathogenic biofilms that spread infection. As was the norm at such meetings, Christian's lab talk prompted a probing discussion of experimental protocols and preliminary results. This discussion began with a series of questions directed at Christian, but it was not long before I noticed that the murmurs, comments, and questions had coalesced into two very separate conversations. The first, to my left, was between several of the members of the Centre who had backgrounds in biology, Malcolm, Peter (both lecturers), Martin (the Centre Director), and Christian. They turned towards each other and began a discussion of the biological details of Christian's experiments and the ways in which they could be improved.

Grant (a lecturer with a background in electrical engineering) sat beside this group, but rather than join the discussion his attention was focused on disassembling and reassembling his pen. I watched with interest as he did this for several minutes before looking up, clearly mulling something over.

[34] A doctoral student who had come to synthetic biology via an undergraduate degree in biology in which he specialised in biochemistry, before subsequently moving into the synthetic biology masters and then doctoral programmes.

[35] The adoption of engineering terms into the language of synthetic biology shall be discussed in chapter four.

However, rather than direct the questions and comments he was formulating towards Christian, Grant turned in his seat towards two other men who are considered, within the dichotomous divisions of the Centre, to be on the engineering side, David, a doctoral student hailing from biotechnology, and George, a postdoctoral researcher with a background in mathematics. Grant then proceeded to engage David and George in a discussion of the engineering potential of Christian's work. I sat perfectly positioned between these two conversations, marvelling at their separation and varying content. Not a single question was shot across the divide, and at no point during the remaining discussion time did these two conversations merge into one. The question arose for me then, as it has so many times, how can we understand the division between the engineering and biological sides of synthetic biology? A division that persists within a discipline that is so clearly and explicitly dedicated to interdisciplinarity, to becoming hybrid.

A hybrid endeavour

As addressed in chapter one, there has been a general shift towards interdisciplinarity in recent decades. Budtz Pedersen (forthcoming) explores this shift as it affects science and innovation, highlighting that a large amount of funding has been poured into the endeavour in recent years from a variety of sources.[36] According to a 2005 report from the American National Academy of Sciences, entitled *Facilitating Interdisciplinary Research*, there are however a number of drivers for this current interdisciplinary turn in science and innovation, other than simply funding. It states that, "[i]nterdisciplinary thinking is rapidly becoming an integral feature of research as a result of four powerful drivers: 1) The inherent complexity of nature and society; 2) The desire to explore problems and questions that are not confined to a single discipline; 3) The need to solve societal problems; and 4) the power of new technologies" (National Academy of Sciences 2005: 40). Synthetic biology is

[36] A prominent example being "Horizon 2020," the European Union's framework programme for research and innovation which has a total budget of €7billion (2014-2020).

motivated by all four of these drivers and, as such, the relationship between biology and engineering is seen as vital to its endeavour (Andrianantoandro et al. 2006; Endy 2005; Heinemann and Panke 2006; NEST 2005). Yet synthetic biology doesn't just desire to be interdisciplinary in its approach; as discussed in chapter one it wants to go further and become a hybrid discipline.

It is this hybridity that is hailed as promising both a new approach to biology, which shall be discussed in chapter six, and a way of overcoming the "failures" of biotechnology (Heinemann and Panke 2006). Yet, despite being framed as unproblematic (Andrianantoandro et al. 2006), forging this promised hybrid discipline of biology and engineering requires the reconciliation of two fundamentally different approaches. This chapter thus aims to address this conundrum through an exploration of the relationship between engineering and biology and an examination of what, I argue, can be seen as synthetic biology's constituent epistemic cultures, in order to ultimately examine what is going on 'under the hood,' as it were, of the attempts to establish synthetic biology as a new discipline.

The Oxford English Dictionary defines 'hybrid' as "anything derived from heterogeneous sources, or composed of different or incongruous elements" (OED 2009). Touching on the essential disparities between synthetic biology's incongruous elements, Ferber writes "[t]his fledgling field, which is attracting engineers and biologists in equal measure, means different things to different people. Engineers view it primarily as an engineering discipline, a way to fabricate useful microbes that do what no current technology can. But many biologists see it instead as a powerful new way to learn about cells" (2004b: 158). Such differences are hardly surprising given that engineering and biology have traditionally been very different fields, with very different goals. As Vincenti writes:

> "[e]ngineering research . . . has as its ultimate goal the production of knowledge useful for design (as well as production and operation); scientific research aims basically at explanation and understanding. As a result, research in engineering is pursued with

> different priorities and attitudes and remains more intimately tied to specific devices. It emphasizes application rather than illumination" (1993: 231).

Thus Vincenti (1993) argues, as Rheinberger (1997) and Keller (2009b) do, that such significant differences between engineering and science should not be ignored.

Yet, as Keller asserts, synthetic biology denies, at least tacitly, that there is any such meaningful distinction between engineering and science (2009b). Synthetic biology is, she argues, the poster child of technoscience. A site where knowing is making and making is knowing, where the boundary between science and engineering, representing and intervening, blurs to such an extent that it does not make sense to speak of them as separate. Yet, to speak of science and engineering as being essentially the same is a step too far, according to Keller. She writes, "[w]hile there may be - arguably, even can be - no looking without touching, it does not follow that looking and touching are the same" (2009b: 294). Furthermore, Keller asserts, such a dissolution of their differences, erases not only disciplinary boundaries, but also a variety of conceptual aims which, she argues, still retain differences that need to be marked (2009b).

Such differences in conceptual aims can, I believe, be explained and explored using Karin Knorr Cetina's notion of 'epistemic cultures' (1999). An epistemic culture, according to Knorr Cetina, refers to the sets of practices, arrangements, and mechanisms that comprise a culture's attitude towards knowledge and its way of justifying knowledge claims. These practices and beliefs are shaped by affinity, necessity, and historical coincidence, and ultimately determine how we know what we know. In her work on epistemic cultures, Knorr Cetina highlights the disparities between two cultures of knowing, molecular biology and high-energy physics. Knorr Cetina describes epistemic cultures as thriving "in internally referential systems," noting that "[s]cience and expert systems are obvious candidates for cultural division; they are pursued by groupings of specialists who are separated from other experts by institutional boundaries deeply entrenched in all levels of education, in most research organizations, in career choices, in our general systems of classification" (Knorr Cetina 1999: 2). Knorr Cetina explores the epistemic cultural differences between molecular biology and high-energy physics in terms of their relationship to the empirical, their enactment of object relations, and the nature of their internal social relations. Through her explication of these differences Knorr Cetina ultimately challenges the previously accepted view that the sciences are all part of a unified pursuit.

In developing the concept of epistemic cultures, Knorr Cetina drew on the work of anthropologist Clifford Geertz, adopting the idea of 'symbolic structurings' as a way of bringing a sensitivity for symbols and meaning to the study of practice. Consequently, she follows Geertz in defining 'culture' as "an historical transmitted pattern of meanings embodied in symbols, a system of inherited conceptions expressed in symbolic form by means of which men communicate, perpetuate, and develop their knowledge about and attitudes towards life" (Geertz 1973: 89). Knorr Cetina carries the focus on practice inherent in this definition of culture into her use of 'epistemology.' "The issue," she writes, is "to recover 'epistemology' from studying finished products (restrictively defined as scientific theories)" and instead "concern epistemology with process – with the concrete, mundane, everyday practices of inquiring and concluding through which participants establish, for themselves and for others, knowledge claims" (Knorr Cetina 1991: 108), practices which Knorr Cetina refers to as epistemic machinery.

Two distinct epistemic cultures

The epistemic machinery, or machineries of knowing, within an epistemic culture thus affect everything from the way its members communicate, define entities, and classify things, to the methods they use, their epistemic strategies, and their ways of collaborating. As noted above, Knorr Cetina contends that scientific disciplines and expert systems, such as biological science and engineering, are obvious candidates for epistemic cultural division. However, before exploring the differences and divisions between these two, and the role they are having in shaping the Centre and the emerging discipline of synthetic biology, let us briefly explore what engineering and biology are, and why we can see them as two distinct, epistemic cultures.

Epistemic cultures, like all cultures, develop and change over time. Practices and concepts which were at first new, revolutionary even, become mundane and taken for granted. They become the epistemic machinery that shapes the emerging epistemic culture and come to define it and what counts as knowledge for those within it. Thus it is important to be clear about what is meant when I speak of engineering and biology.

Engineering

Engineering, at its most basic level, can be defined as "the creative application of scientific principles to design or develop structures, machines, apparatus, or manufacturing processes" (Engineers' Council for Professional Development 1947). This definition may seem self-evident to some, but it may also jar with others. It encompasses much of what we think of as engineering, but it sets the discipline apart from what came before it and, as so often happens with such things, it now seems a little out-dated. To briefly explain what I mean we must look back to the second half of the nineteenth and the early twentieth centuries. It was at this time that, through the adoption of scientific and theoretical methods, engineering shifted away from being a traditional craft enterprise. Historian of technology Robert Buchanan writes of the development of engineering that, "[w]hat had still been essentially a traditional craft based upon the acquisition of skill by practice as late as the Great Exhibition of 1851, was converted by the outbreak of World War I in 1914 into a sound theoretical discipline based on scientific principles, albeit in a highly practical context" (1985: 229). According to Divall, the practices and concepts that saw engineering being performed and presented as an efficient, systematic and rational enterprise, rather than a messy, intuitive one, implemented through trial and error, arose at this time following a concerted effort to adopt the methods of academic science.[37] A shift that was motivated, at least in part, by a desire for the new discipline of engineering to be viewed as a legitimate academic pursuit and profession (Divall 1990).[38]

This systematic, theoretical approach has, regardless of its original motivation, become a defining feature of engineering[39] and, I would argue, the belief in it is a key element of its epistemic culture. Yet, despite this focus on the incorporation of scientific knowledge, engineering remains a very practical endeavour. Vincenti, an aeronautical engineer turned historian of technology, contends that the practical work of engineers is always aimed at achieving a utilitarian end, and as such can be divided into three main tasks; the design of artefacts, the construction or production of artefacts, and the operation of artefacts to meet a recognised need. The different branches of engineering can therefore be seen to arise from the application of these tasks to varying aspects of the physical world. Resulting in the likes of electrical engineering, mechanical engineering, civil engineering, and chemical engineering, a far from exhaustive list as the disciplines and sub-disciplines of engineering spread across an impressive range of specialities.

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[37] However, this vision of engineering as a rational, efficient, and systematic endeavour does not, according to Bucciarelli (1994) (himself an engineer turned ethnographer of engineering), capture how engineering is really practiced, but rather how it presents itself. Bucciarelli (1994) argues that engineering is, in practice, much messier and more reliant on trial and error than engineers usually acknowledge. Likewise Petroski notes that "Modern engineering is a more highly mathematical and scientific endeavour, but its practice still requires a good deal of commonsense reasoning about materials, structures, energy, and the like" (1996: 2).

[38] Noble outlines that throughout the nineteenth and early twentieth centuries, the classical US colleges chose to explore science at a solely theoretical level and thus opposed the development of technical education. However as the development of the machine and the railroad industries intensified, so too did the demand for engineers. This demand ultimately led to the establishment of technical education outside of the classical colleges in the US with the aim of teaching the practical application of science. Nevertheless, the classical colleges were still resistant to the teaching of engineering, and while empiricism was eventually introduced into the classical colleges' science courses, engineers were deemed to be second-class scholars (Noble (1977). Thus, Divall contends, adopting science's systematic and theoretical approach was a conscious attempt to shed this second-class status and legitimise the discipline (1990).

[39] As can be seen in contemporary engineering literature (e.g. Pahl et al. 2007).

However, to return to the Engineers' Council for Professional Development definition above, if we think of contemporary engineering as being the scientific and theoretically-based design, development, and operation of artefacts, where modern engineering has moved away from this definition is not so much in terms of this process and these practices, but rather in terms of the artefacts themselves. Since this definition was written in 1947, engineers have increasingly broadened their focus from the inanimate objects encompassed within the definition ("structures, machines, apparatus," and "manufacturing processes") to the world of animate objects. As shall be discussed in chapter six, attempts to apply some form of an engineering approach to biology date back at least as far as the 1860s, yet it was not until 1936 that the term biological engineering was introduced[40] (Compton and Bunker 1939). Since this time several engineering sub-disciplines and related disciplines have emerged at the intersection of biology and engineering including biomedical engineering, molecular engineering, biomolecular engineering, protein engineering, tissue engineering, biochemical engineering, and genetic engineering. As such, it would seem that biology has become the new frontier for applications of engineering's concepts and practices. Nevertheless, as shall be discussed below, it is not always a hospitable frontier to the notions and approaches of the engineer.

Biology

Most, if not all, are familiar with the discipline of biology, but as with engineering, the study of life has not always taken the form we think of today. As shall be discussed in chapter six, according to Foucault (1970) biology did not even exist before the nineteenth century, acquiring it's modern usage in 1802. Since this time the scale at which life is examined has shifted

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[40] Biological engineering was used to denote a new branch of biology taught at MIT, which would utilise basic knowledge of physics, mathematics, chemistry, and several fields of engineering. The MIT Biology department's name was even changed to the Department of Biology and Biological Engineering in 1942, however this only lasted until 1944 when the name was changed back to the Department of Biology (MIT).

significantly, as has the language used to describe life and the methods used to scrutinise it (a history which will also be addressed in chapter six). But, since its inception, biology has maintained a focus on life and living organisms, and an emphasis on understanding the processes of life. Biology as a field of study is vast and eclectic, covering the structure, function, growth, evolution, distribution, and taxonomy of all living organisms, thus it has long been divided into sub-disciplines or branches. These branches, like the branches of engineering, indicate various specialities of focus, either in terms of the kinds of organisms studied (for example botany and zoology) or in terms of the scale or level of organisation at which organisms are studied (such as molecular biology, physiology, and ecology). Yet, despite the broad scope of biology, there are certain concepts that govern and unify all biological study and research. In general, biologists identify the cell as the basic unit of life, the gene as the basic unit of heredity, and evolution and adaptation as being the basic mechanisms by which species develop, change, and survive. It is also understood that all organisms share certain characteristics; they respire, consume nutrients, excrete, grow via assimilation, respond, move, and reproduce (Roberts et al. 2000). Thus, aside from their obvious differences in focus, a significant disparity between engineering and biology is their relationship to knowledge.

Where engineering is focused on designing, building, and operating artefacts, biology is focused on understanding life and it's processes. Vincenti addresses the differing relationships of science and engineering to knowledge in his 1993 book, *What Engineers Know and How They Know It: Analytical Studies from Aeronautical History*. He contests the notion that engineering, as a discipline, simply applies the knowledge that science reveals. Technology, he asserts, may "apply science," however this is not the same as claiming it is "applied science." Engineering, he contends, is an "autonomous body of knowledge, identifiably different from the scientific knowledge with which it interacts" (Vincenti 1993: 3-4). For scientists, he asserts, knowledge is an end in itself and the central objective of their profession, whereas for engineers, knowledge is a tool, a means to a utilitarian end. This disparity seems to create a space for collaboration; wherein engineers could use the knowledge obtained by biology as a tool to achieve a utilitarian end. However despite many attempts, such a successful collaboration has, until recently, proven difficult to achieve (2002).

As mentioned in chapter one and discussed in chapter six, synthetic biology is one of a growing number of emerging disciplines, which are attempting to colonise this collaborative space between biology and engineering. As biology as a whole becomes increasingly interventionist we are seeing more and more disciplines which have 'buy-in' from both biologists and engineers. However, as in the relatively unsuccessful attempts at combining the disciplines addressed by Keller (2002), tensions, misunderstandings, and miscommunications still arise.

Epistemic cultural differences within synthetic biology

> *To some extent they are very definitely two tribes*
> (David, doctoral student, biology)

In public, synthetic biology is so often framed as the unproblematic and systematic assimilation of engineering and biology. Indeed my fieldnotes are filled with examples of Malcolm and Alan's (the Centre Directors) presentations to groups both inside and outside the university[41] where any and all tensions are glossed over in favour of presenting synthetic biology as a harmonious, straightforward endeavour. According to one such presentation, rolled out for every group visiting the Centre, the straightforward process of designing and building a synthetic biological 'product' is analogous to the engineering of a BMW. The parts used in both cases, according to Alan, are equally high spec, controlled, and standardised, and slot just as easily into their awaiting chassis. While the work to achieve this ends is undertaken by a coherent group of synthetic biologists. Yet such presentations so often jarred

[41] Presentations to the likes of prospective students, new students, potential industry partners, academics from other universities, the Guild of Worshipful Engineers, and government representatives, the list could go on and on.

with my observations behind the Centre's closed doors, where not only technical difficulties, but also differences and tensions between the two 'sides' of synthetic biology, were apparent.

So, to return to the lab meeting with which I started this chapter, how can we understand the events using the concept of epistemic cultures? To begin with I wish to assert that the members of the Centre, and indeed of synthetic biology more broadly, hail from two distinct epistemic cultures associated with biology and engineering. Two internally heterogeneous but coherent groups of participants who find much more in common with other members of their own 'group' than they do with the members of the other 'group.' In some ways the existence of these two 'groups' defies logic. Especially when one considers those participants in synthetic biology who have had interesting trajectories into the field, weaving between the life sciences and the more 'engineering' disciplines. Yet, even those within the Centre with such interesting backstories defined themselves as belonging in one 'group' or the other, identifying themselves more closely with members of one 'group' or the other and describing the discipline as consisting of two separate 'groups.' Furthermore, and as I shall discuss below, I observed key differences between these so called two 'groups' that support the notion of their existence whether that existence is logical or not.

Indeed I found the 'biologists' to have more in common with each other, than with the engineers, when it came to their research questions, methodologies, organisation, time frames, patterns of collaboration, relationships with data and experimentation, and required skills. I also found them to share language, research objects, a common knowledge base and, according to several of the members of the Centre, a 'world view.' All of which differed from those of the 'engineers,' who likewise shared commonality with each other, and all of which shaped the day-to-day work of both groups.

As I watched members of the Centre interact with colleagues from the other 'side,' this cluster of differences became apparent, leading me to wonder whether we can view these two groups as distinct epistemic cultures. Clearest amongst the differences I identified (which I shall evidence below) was the lack of a shared knowledge base between the biologists and the engineers. Each of the epistemic cultures had their own distinct systems of classification, their own conceptions of their research entities, their own empirical procedures, and their own epistemic strategies, all of which had produced, through time, very different bodies of knowledge. Yet, here they were attempting to collaborate with each other on projects that drew from the strengths of both sides, without, in some cases, even the most basic knowledge of each other's discipline.

Unshared knowledge

I first met Grant at the Centre's inaugural annual symposium where people from the Centre, and invited guests from the international synthetic biology community, spoke to an audience of interested parties (including, among others, fellow synthetic biologists, doctoral students, university colleagues, funding bodies, and potential industry partners) about their work and the goals of the Centre and the discipline. I had arrived after much of the lecture theatre, in which the symposium was taking place, had already filled and claimed the last seat in a row, next to a friendly-looking, bespectacled man in his mid-thirties. It soon became apparent that he knew very little biology as, after establishing that I had a background in biochemistry, he spent the morning quietly seeking my help to understand the presentations. Grant was an electrical engineer by training, and a very skilful one at that, but he had never studied biology and felt he had a lot of ground to make up.

So, after attending his first journal club meeting, where he listened attentively and took copious notes, he again sought my help to comprehend the biology, inviting me back to his new office in the empty, un-renovated shell of what would soon become the overcrowded Centre's hub. Sitting on his desk was a copy of *Essential Cell Biology,* a basic biology textbook that Grant was systematically working his way through, chapter by chapter, and it was this that he now consulted as he asked me to explain the journal club paper to him. "*What,*" he asked, "*were 'oligos' and primers, and how exactly did PCR work?*" Oligonucleotides, primers, and Polymerase Chain Reaction, while understandably confusing for someone without any biology training, would be seen as entry-level knowledge for someone from the biology side of synthetic biology, and yet they were things that Grant had never encountered before.

This degree of unfamiliarity with biology and experimental work was frowned upon by the biologists, as it was believed to result in the engineers having unrealistic expectations for what could be achieved using biological materials. Grant was new to the field and working hard to overcome his lack of experience but, as Martin highlighted, a lack of biological knowledge was prevalent among even the most senior engineers involved in synthetic biology. As Martin explained it:

> *So some of us have come to it from biology and gone OK yeah, we want to now incorporate the engineering side because it does make more sense, we want to actually build things and do this in a predictable way, and for that we have to thank those who've come in with engineering ideas. But you know every now and again you have to slap them* [Laughs]. *So a lot of what Drew Endy says kind of doesn't make sense when you go down to the biology in the everyday wet lab, and it's exactly the same with Jim Collins, and it's because neither of them could actually go into the lab and start doing these experiments, because they never did, you know, they've never really done them, especially Jim. I mean Jim Collins has this amazing lab doing all this biology but he's never done an experiment.*
>
> (Martin, senior researcher, biology)

Yet, despite his unfamiliarity with biology, Grant was still expected to plough forward with modelling biological constructs. Thus, while shadowing David for a day, we encountered Grant as he and a synthetic biology Masters' student, Anita (hailing from an engineering undergraduate degree), attempted to design a model for a toggle switch system that involved the use of microarrays. On seeing us across the computer lab, Grant rushed over to seek David's help in understanding how microarrays work. The problem was that neither Grant nor Anita had ever seen, let alone performed, a microarray.

Grant had looked it up on Wikipedia but wanted to check if he had understood it correctly. He couldn't figure out what was used as a control, how many RNAs[42] bind to each probe, or whether it would give you meaningful data if the toggle switch was in a static state. While David patiently gave Grant a crash course in microarrays I wondered what effect the kind of lack of experience Grant and Anita displayed with microarrays, and the underlying lack of biological knowledge, would have on the models being designed for synthetic biology by engineers.

Many months later I found a possible answer to this question as I spent the day shadowing Janet, helping her in the lab where I could and discussing the various 'goings-on' of the Centre. As we sorted out the contents of an overloaded laboratory freezer, separating well-labelled and useful samples from those considered superfluous or whose contents was a mystery, the conversation turned to the doctoral project Simon (a student with a background in bioinformatics) was planning.

We had been discussing the biology/engineering divide within the Centre (something that many members of the Centre were keen to discuss with me) and Janet had commented that overall the engineers within the Centre were "*getting better*" and becoming "*more realistic*." By which she meant they were gaining more knowledge of biology and as a consequence their ideas about biology were, to her mind, less simplistic and unrealistic. However this improvement, she was quick to add, was not across the board. Grant, she noted was trying hard to understand the biology he was working with and was, according to Janet, becoming a better synthetic biologist for his efforts. However, Patrick (a theoretical physicist by training who was now working primarily in biomathematics in association with the Centre) was, according to Janet, the most removed from reality and Patrick was to be Simon's doctoral supervisor.

[42] Ribonucleic Acids.

Patrick was suggesting that Simon's doctoral project should involve an attempt to build a more complex version of the repressilator,[43] one with six genes rather than three. He was, apparently, basing this advice on the work of one of his previous doctoral students who had already modelled the system and had shown that the six different genes of the proposed, upgraded, repressilator would 'just' be required to have expression levels within 10% of each other. At this point in her account Janet laughed aloud. While 10% clearly sounded like a workable margin of error to Patrick and his engineering-based student, Janet noted that she would not be able to achieve this degree of uniformity even if she had six copies of the same gene. With six different genes it was nigh on impossible.

This disparity, between the parameters of the model designed by an engineer and the biological 'reality' as viewed by a biologist, was interesting. Janet clearly believed that Patrick and his student did not have sufficient understanding of the biology to model it in a meaningful and useful manner from an experimental perspective. While Patrick clearly believed his student had developed a model that could be used as a road map to meaningful experimental data. This example not only highlighted the lack of shared common knowledge between the engineers and the biologists, but also their very different relationships with experimentation, data, and models.

Contentious models

The accuracy, applicability, and usefulness of models were common topics of conversation within the Centre. For example, while discussing the unrealistic conditions that some engineers assume for their models of biology, David humorously explained that it was the equivalent of them assuming "*that the chicken is round and is in a vacuum*." Such attitudes and differences of opinion over the role and usefulness of models was the occasional cause of tension and frustration between the engineers and the biologists within the

[43] A synthetic, genetic regulatory network, which was an early and highly significant synthetic biology project reported on in Elowitz and Leibler (2000).

Centre. Peter, one of the iGEM team advisors, recounted for me the following example, which demonstrates this tension.

> *I remember an argument about this occurring between people in the iGEM team where the advisor was telling the student to model cell growth, and he just said, 'model it by just making a sphere grow bigger. It just gets bigger and bigger.' And the student was like . . . 'but that's not how it works, so why model it that way if it's not how it works?' And the engineer was like, 'it doesn't matter, it will give you something that will be a model for cell growth.' And she was like, 'yeah, but it'll be meaningless because it's not how it works.' And they never resolved it, you know. They both thought each other was stupid.*
>
> (Peter, senior researcher, biology)

This argument illustrates both the frustration and conflict that occasionally arose between the two sides of synthetic biology, and also the differing notions of what counts as meaningful data - what makes sense for the model or what makes sense for the biology? It would seem that the biologist in the above example considers a model that is not a close reflection of reality to be meaningless, and thus any data generated by it to be equally meaningless. Whereas, it would also seem that the engineer is adhering here to the notion of the 'good enough' model.[44] In engineering, after all, the aim of creating a model is not to recreate reality, but rather to devise something that is simpler and easier to work with than reality, but that is still close enough, or 'good enough,' to provide meaningful data. Using this principle, engineers revisit and revise models if the data produced is not considered to be sufficiently meaningful.[45]

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[44] For a discussion of 'good enough' modelling see Bach (1997).

[45] As Favre (2004) argues, a model could be considered to be good enough, until it is shown that it provides bad answers about a given situation.

David also spoke to me about this tension on a separate occasion, and his explanation goes some way to clarify the basis of the conflict recounted by Peter. "*Approximations*", David said, "*just do not work in biology*." This, he claimed, set biology apart from the physical sciences that the engineers were more familiar with where "*assumptions and approximations can be plugged into equations and be useful. But, in biology*," he continued, "*biologists will just say, 'but that is not how it is in reality, so the results are meaningless'*" (David, doctoral student, biology). I do not wish to debate whether assumptions and approximations are useful or useless within biology, but it was very clear, from both of these accounts and other events during my fieldwork, that this issue was a bone of contention within the Centre.

The engineers were, however, largely aware that the models they produced were contentious and that there was a need to improve their accuracy. However even these efforts could be viewed by the biologists as having uncertain value. For example, I spoke to Janet while she was in the middle of writing part of a funding proposal, one that was being submitted by a multi-institutional group of modellers, including Grant. Janet was, as she put it "*the token biologist*," but when I asked her what the proposal was about she told me she didn't really understand it herself. That is, except to say that it was about trying to develop a modelling tool that would separate out linear and non-linear variability in order to make the design and modelling of synthetic biology parts more accurate. The aim was, she thought, "*to figure out in a biological system which knobs were too complex to fiddle with and which ones we know enough about that we can use them to tune the system*." However, she immediate commented that she wasn't sure we know any parts well enough to be able to use them to tune the system. Yet despite her misgivings about the feasibility of the project Janet had chosen not to raise them with her engineering colleagues.

Janet explained that the difficulty with highlighting problems with the modelling approach within synthetic biology is that you so easily get called a naysayer biologist who just thinks biology is too hard to model. The notion of the 'naysayer biologist' comes from the judgement by some engineers that biologists do not know enough about engineering and modelling in order to determine whether or not biology is 'too hard to model or engineer.' I heard the refrain several times from engineers that biology is not as complicated as biologists like to think it is, as it is no more complicated than many of the materials and systems that engineers have successfully modelled in the past. The reason the engineers gave me for the biologists' misapprehension was their unfamiliarity with both engineering and modelling.

To make this point Stephanie recounted a recent visit she had paid to a polymer plant where she was telling an engineer about a model she was trying to construct of the Golgi apparatus,[46] which has many different 'species' and potential behaviours. The engineer responded that it sounded just like modelling polymers, except that polymers have more possibilities and more 'species.' This, Stephanie said, just goes to show that engineers are not unfamiliar with complexity, and that, despite what some biologists believe, complex systems absolutely can be modelled. Stephanie put some of the biologists' apprehension about models down to their unfamiliarity with the ubiquity of modelling in the modern world. Using the takeaway cup of coffee she held in her hand to illustrate her point, Stephanie explained that from the beans to the cup, all of the processes had been industrialised and each step would have been modelled. Each piece of technology, and every industrial product, she went on, has been through modelling. Thus, given that modelling is everywhere, and is deemed useful in so many areas, Stephanie exclaimed that she really could not understand why biology would be any different or why biologists are so reluctant to embrace it. The only possible explanation, as she saw it, was that "*Biology is the poor, backward cousin, lagging behind Chemistry and Physics, both of which have embraced engineering and modelling*" (Stephanie, senior researcher, engineering).

The paired stereotypes that underlie these conflicts over the importance and usefulness of modelling, those of the backward biologist and the ignorant

[46] The Golgi Apparatus is an organelle found within most eukaryotic cells. It has a central role in the modification and packaging of proteins for transport around or outside of the cell.

engineer, are arguably neither fair nor helpful in the formation of a functioning hybrid discipline. Yet, they do help to indicate the division and differences between the two epistemic cultures within synthetic biology. As indicated above, these differences are observable in the knowledge base of the two sides of synthetic biology and also their attitude towards, and expectations of, mathematical models and biological material. Another place that the epistemic cultural differences between engineers and biologists, within synthetic biology, are visible is in their expectations of each other's work time frames.

Time frames

> *Yeah it's tough when they* [engineers] *don't get it, when you're like, 'yeah this didn't work because the cell got a mutation and evolved,' and they just stare at you like, 'what? Fix it!' . . . Which is a good view, but not one for like, fix it for next week. But yeah, it would be good, I'll bear that in mind, next decade let's have an engineered cell that doesn't evolve and an engineered cell that behaves, right?*
> (Martin, senior researcher, biology)

As the above quote indicates, the lack of basic familiarity with, and understanding of, each other's disciplines also affected the synthetic biologists' appreciation of each other's workable timelines. This is arguably what underlay the engineer's request that Martin "*fix*" the cellular mutation immediately. A fix that the engineers were probably unaware would take many, many hours of lab work.[47] Yet, this lack of understanding of workable timelines cut both ways.

Lewis, a doctoral student hailing from engineering, has embraced both laboratory and modelling work within his project, and has both a biologist and an engineer as supervisors. While he strives to successfully combine synthetic biology's two sides he struggles at times with the expectations of his

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[47] A lack of awareness that is not entirely surprising given synthetic biology's rhetoric that suggests cells can easily be designed and controlled.

supervisors, who have, he believes, unrealistic expectations for how he will divide his time between the two sides of his work. According to Lewis, Martin, his supervisor from the biology side, does not seem to appreciate how much work and time is involved in modelling, claiming that Lewis should only need to spend one hour on modelling for every ten hours he spends in the laboratory.

Lewis, who believes that his modelling and laboratory work require equal amounts of time, described modelling as being creative, and requiring a lot of thinking, which he conceded, may not look like 'work' to a biologist who is used to doing practical tasks in the laboratory. Yet he also noted that modelling work is a lot more immediate, explaining that when you have a good idea for how to do something in a model, you can immediately check the equations to see if it will work. Whereas in biology, if you come up with a new idea for how to do something, you then have to do all of the lab work in order to see how it functions, and this can take quite some time, a fact that is not always appreciated by his engineering supervisor.

The incorrect assumptions, on both sides, about the workable time frame for any particular task on the other side, are arguably due to the unfamiliarity and lack of experience the two sides have with each other's work. However, these assumptions are also influenced by the weight individuals place on the importance of the work done by each of the two sides of synthetic biology. Lewis addressed this point in relation to his two supervisors, each of whom, he felt, clearly viewed their own 'side' of the discipline, and it's inherent goals, as central to synthetic biology's endeavour, with the other discipline playing a supporting role. Lewis encountered these biases in his interactions with his supervisors regarding his doctoral project. Lewis felt pressured by Martin to quickly complete, what Martin saw as, the 'supporting' modelling work so that he could get on with the 'important' work of biological experimentation and discovery. While Grant encouraged Lewis to focus on the 'important' and 'central' modelling work, testing biological feasibility when required with the view of improving the model. Interestingly Kwok noted a similar attitude, quoting Christina Agapakis (then a grad student at Harvard Medical School doing synthetic biology research and now the creative director at organism design company, Gingko Bioworks) as saying, "there's a lot of biology that gets in the way of the engineering" (2010: 288).

This lack of understanding of each other's discipline is, according to Malcolm, a result of the members of the two hemispheres of synthetic biology having been trained in different ways of thinking and in distinct approaches to research.

> *The disciplines tend to be taught in different ways. So the biologists' . . . they're not there to solve problems, you know, engineers solve problems, biology, biochemistry are there to explore hypotheses, looking at fundamental mechanisms, work out how things work,* [they] *are driven by . . . fundamental knowledge generation I suppose, and an engineer's there to solve problems, there to build things, do things, make things happen. So that's a very different way of training, so you've got two communities that have been trained in very different ways . . . that's challenging, to bring that together.*
> (Malcolm, senior researcher, biology)

Malcolm's acknowledgment that training plays a significant role in the generation of distinct academic communities, echoes Knorr Cetina's assertion that epistemic cultural divisions are deeply entrenched in all levels of education. For it is through their education that the members of each of these groups have learnt to prioritise certain goals and ask certain research questions, goals and questions that differ from each other. It is also through their training that they have learnt to speak the distinct language of their discipline, of their epistemic culture.

Language

Language use, like knowledge base, attitude towards modelling, research priorities, and ideas about time scales, acts to set the two sides of synthetic biology apart, again demarcating them as separate epistemic cultures. Firstly, and perhaps most obviously to anyone venturing into the world of synthetic biology, there is the problem of jargon. There is a fair amount of shared terminology and jargon within the lexicon of this emerging discipline, biobricks, chasses, parts, devices, and systems being the most obvious examples.[48] But there is also a fair amount of unshared language, and it is this that can make comprehension difficult for all. As Lewis said, in regards to meaningful communication between engineers and biologists:

> *It's difficult because like each discipline has their own jargon and stuff, so it's sort of like . . . 'sorry, explain what that means?' And it's like, 'you know! Oh, of course, you don't understand what I mean.'*
> (Lewis, doctoral student, engineering)

As Lewis addresses, members of both sides of synthetic biology can be guilty of assuming, like arrogant tourists abroad, that everyone speaks their language. Forgetting that both the words they use and the concepts these words denote may be completely foreign to their collaborators and thus require patient translation and explanation.

I remember sitting in the audience of a RoSBNet[49] workshop in Oxford listening to back-to-back talks from biologist Michael Hecht and electrical engineer Murat Arcak. Hecht presented an artificial molecular parts kit, and Arcak discussed the synergistic relationship between synthetic biology and control theory. These two men used strikingly different languages and presentation methods to convey their work. Arcak's slides were full of mathematical equations, models, and diagrams (matrices), while Hecht's talk and slides centred around protein diagrams, pictures of petri dishes, eppendorfs, and protein sequences. Yet, both men clearly assumed that their talks were straightforward and simple. Hecht's complex biological presentation, for example, was filled with comments like: "*we all know . . .* ," "*this is simple stuff*," "*the electrical engineers in the room will all get this*," and "*this is biochemistry 101*." While halfway through Arcak's talk, a talk dominated

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[48] The engineering discourse entering synthetic biology is discussed in greater detail in chapter four.

[49] RoSBNet stands for Robust Synthetic Biology Network.

by complex mathematical formulas, he said, much to my amusement, "*this is the only slightly technical element of the talk*."

After Arcak's talk, Janet and I looked at each other with shared incomprehension, and she, a senior synthetic biology researcher, commented that she was impressed that I had been taking notes at all during the talk as she had no idea what was going on. Whereas Grant (also a senior synthetic biology lecturer and researcher), who had struggled through Hecht's talk, commented that Arcak's presentation was from his world, and was the way that he looks at things. The specialised nature of the content of both talks was obviously a hindrance to their widespread comprehension by even experienced members of the mixed synthetic biology audience. A situation which further illustrates that the two sides of synthetic biology do not have the shared language requisite for a shared body of knowledge. Both speakers employed a lot of jargon and terminology in their talks that would have been unfamiliar to at least some, if not half, of the audience, and yet they did not explain themselves at all, assuming, incorrectly, that everyone would understand them.

Nevertheless, as Grant stressed on another occasion, the difficulties with comprehension within synthetic biology are not only due to the use of 'foreign' words and concepts, as was the case with these talks, but also due to variations in the use of the same words.

> *Engineers and biologists do not necessarily speak the same language, in the sense that the vocabulary is not necessarily the same, and the level of precision is not the same either.*
>
> (Grant, senior researcher, engineering)

Grant, who would often find himself lost in conversations with biologists, especially early on, mentioned the issue of precision to me several times. He stressed that in engineering, words are given precise meanings and when they are used, they always mean the same thing, and when someone means 'that' thing they always use 'that' word. Whereas, in his opinion, biologists are a lot less stringent and will use multiple words to mean the same thing "*just for* *variety*." This decision to, as Grant saw it, make their writing more interesting rather than clearer, confused and frustrated him. Meanwhile Grant's frustration and confusion amused Janet. However despite her amusement, Janet conceded that this variation in word-usage, where the biologists and engineers take a word to mean different things, could also lead to problems.

> *I think the bigger problem is that people think they know what other people are saying but they don't actually know, and so then, you know, you find out six months later that . . . 'I thought you said this but actually what you meant is that,' and you know, now we've kind of gone round in circles several times.*
>
> (Janet, senior researcher, biology)

Thus variations in language use, and the resulting misunderstandings, are not only an indicator of epistemic cultural difference, but also a potential impediment to successful collaborative work.

Spatial and conceptual separation

Potential fuel for this misunderstanding, which, as Janet notes, can be maintained undetected for months, is the spatial separation that exists between the engineers and biologists at the Centre. For while the Centre houses both sides of the collaboration, there exists a disciplinary division nonetheless, with the biologists spending most of their time at the 'bench' in the laboratories downstairs and the engineers spending most of their time at computers in the offices upstairs. This divide is thus embedded into the built environment, with the computers and whiteboards predominantly used by the engineers, and the lab benches and equipment primarily used by the biologists, being separated by a floor and three locked doors. Indeed, even when they are not working, the engineers tend to mill around the upstairs desks, and the biologists around the lab benches and the downstairs office, which contains desks and computers used exclusively by those who hail from biology.

This division continued even when the engineers and biologists were 'working together.' For, while they would meet regularly, they would not work alongside each other. Thus, even when they were working on a common research object, this object would take a very different form for each. Consequently not only did they look at the same words and see different meanings, but they would look with very different perspectives at very different representations of the same research object.

A prime example of biologists and engineers seeing their research objects differently is *E. coli. E. coli.,* and its constituent genes, are perhaps the most common research objects in synthetic biology. Yet, while biologists encounter these objects in the laboratory in their biological form, the organisms smeared in vast colonies on petri dishes (see for example figure 1), or spun down into pellets of cells in test tubes, and the component parts of its genome as bands of black on a Southern blot, for the engineer this same organism and its elements are rendered as a series of data points, it's messy biology reduced to a sequences of numbers. For the engineer it is these numbers that they interact with and interrogate rather than the organism itself, and it is the sequence of numbers that are fed into models, such as the model represented in figure 2.

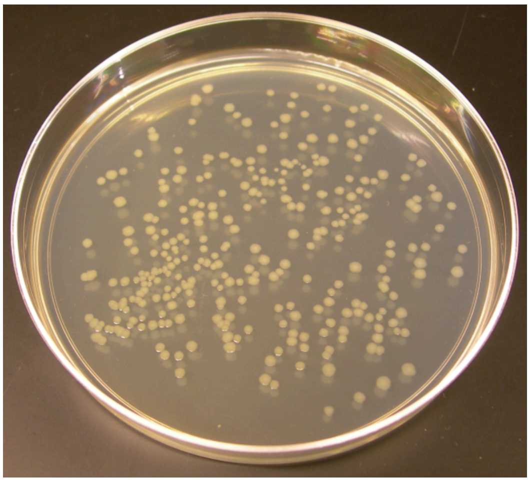

Figure 1: *E. coli* colonies growing on an Agar plate (Ball 2007).

$$\dot{x}_i(t)=f(x_i(t))+\sum_{j=1}^{N} C_{ij}\, g\left(x_j(t)\right),i=$$

Figure 2: A synthetic genetic oscillator system in *E. coli* represented by a nonlinear dynamic equation (Chen and Hsu 2012).

The form that their common research object takes within their work dictates, and is dictated by, the research methods they use in their day-to-day practices. The biologists are generally much more at home at the bench running assays with mutating, reproducing organisms than they are sitting at computers constructing predictive models from first principals, and vice versa for the engineers, who are very comfortable with the inner workings of mathematical formulas but have no idea how to load an electrophoresis gel. As such it is not surprising that the conflicts and misunderstandings mentioned above, between the engineers and the biologists within the Centre, arise. It is perhaps hard for members of both sides to fully reconcile living, reproducing, mutating organisms with predictable mathematical models.[50]

Reconciling synthetic biology's epistemic cultural differences

Thus, what I have attempted to show above is that there exist significant differences between the engineers and the biologists within the synthetic biology research centre where I undertook my research. These differences, I argue, are located within a cluster of disciplinary features, namely their research objects, methodologies, research questions, time frames, relationships with data and experimentation, required skills, language (including their differing strategies of language use – precision versus variety), and their knowledge base. I would contend that these differences ultimately stem from the fact that synthetic biology's parent disciplines, engineering and biology, can be seen as two distinct epistemic cultures. Furthermore, I would maintain that such differences also prove to be obstacles to the formation of synthetic biology as a hybrid discipline.

That is, while this cluster of characteristic differences is arguably constitutive of the epistemic cultures of synthetic biology's parent disciplines, I would contend that, they are also the negative side of epistemic cultures. For it was around this cluster of differences that the tension and conflict within synthetic biology's attempt at disciplinary merging took hold. Given the constituent nature of these features within disciplines, and the current science policy drive towards interdisciplinarity, further examination may find that a

[50] This will be discussed further in chapter five.

similar cluster of epistemic cultural differences proves equally troublesome as others attempt to align themselves with the current science policy drive towards interdisciplinarity.

However, for now let's return to the lab meeting with which I started this chapter, the parallel discussions begin to make sense if we think in terms of the existence of these two epistemic cultures. The members of each of the two conversations were discussing the research questions that interested them, the methods they would use to investigate these questions, and the potential outcomes of doing so, all the time using language, and drawing on a knowledge base, shared with the others in the conversation. These conversations were easy. They required no translation, no simplification, and no explanation. Indeed they required no concession to the 'other side' of synthetic biology at all and thus suffered none of the difficulties of collaboration.

However, despite the ease of such conversations, those within the Centre have, to varying degrees, committed to the synthetic biology endeavour. Thus they have committed themselves to this collaborative effort and, despite their frustrations, I observed that they do try hard to make it work. As such, having established that drawing synthetic biology together can be difficult because it is ultimately a discipline forming at the interface of two distinct and differing epistemic cultures, the remainder of the chapter will explore the attempts that are being made within the Centre to bridge this epistemic cultural divide.

An emerging epistemic cultural community

As mentioned in chapter one, Molyneux-Hodgson and Meyer (2009) argue that central to understanding scientific communities is the need to consider how they change and reproduce over time. Drawing on Gingras' work on the emergence of the physics community in the early twentieth century (1991), Molyneux-Hodgson and Meyer explore the contemporary emergence of a synthetic biology community in the UK and Europe. They argue that emerging scientific communities, such as synthetic biology, "can be analysed through identifying the mixture of movement and stickiness" (Molyneux-Hodgson and

Meyer 2009: 142). Here 'movement' refers to the gathering of what they consider to be the building blocks of a community, such as individual scientists and resources, and the convergence of these building blocks on some central position. They also use the term 'movement' to refer to the articulation of future promises and expectations in order to present the community as being on a trajectory. 'Stickiness,' however, is used here to refer to efforts to tie an emerging community down and together through the likes of specialised associations, conferences, and journals. Devices, that is, that create for the community "a visible, demarcated and powerful niche" (Molyneux-Hodgson and Meyer 2009: 143). At the time of their work, Molyneux-Hodgson and Meyer contended that the synthetic biology community was only just emerging and that it "remains to be seen whether 'synthetic biology' will become a separate discipline with a delineated community of practitioners, a sub-field of one of its constituent parents, or segue into some other configuration" (2009: 143).

Several years have passed since this paper was written and while things have not changed drastically in that time, they have inevitably changed. There are clear examples of the sort of movement Molyneux-Hodgson and Meyer argue is indicative of an emerging scientific community, with a steady flow of both people[51] and resources[52] into the field, and a continual assertion that

[51] The influx of people into synthetic biology has seen a significant increase in the numbers attending the international synthetic biology conference series. Indeed the number of participants has more than doubled since the first conference, SB1.0 in 2004. The first four Synthetic Biology Conferences, SB1.0 through to SB4.0 (held in 2004, 2006, 2007, 2008), had around 1500 participants in total, while the two most recent conferences in the series, SB5.0 and SB6.0 (held in 2011 and 2013) have between them attracted over 1500 participants (BioBricks Foundation).

[52] Large amounts of money continue to pour into the synthetic biology research endeavour. With £20 million worth of research grants announced by the BBSRC in November 2012 (Biotechnology and Biological Sciences Research Council 2012). The EPSRC is another significant contributor to the development of the field, with over £45 million worth of grants currently dedicated to synthetic biology research (EPSRC). The two research councils also paired up towards the end of 2013 to offer £40 million to set up three new multidisciplinary synthetic biology research centres in the UK (Biotechnology and Biological Sciences Research Council 2014). They have also funded a Centre for Doctoral Training in Synthetic Biology, which offers a four-year fully funded doctoral programme for students from the physical and life sciences (SynBioCDT 2014).

synthetic biology is on a promising path towards solving many of the world's ills, while also bolstering the economy (see for example Osborne 2012; UK Synthetic Biology Roadmap Coordination Group 2012). Furthermore, there are increasing signs of the 'stickiness' Molyneux-Hodgson and Meyer contend signals the development of a demarcated scientific community. The international synthetic biology community has, for example, developed a conference series, the SBx.0 series, which is growing in numbers and significance. These conferences are now held every two years and draw upwards of 700 international participants, including some very high profile speakers.

I attended the SB5.0 conference held at Stanford University in 2011, an impressive setting that, in itself, spoke volumes about the growing legitimacy of the field. Sitting amongst hundreds of the leading lights and new disciples of the international synthetic biology community, at the centre of the Stanford University campus in Silicon Valley, it definitely felt like the community was established, recognised, and cutting-edge. Moreover, this is far from the only conference series devoted to synthetic biology. Alongside the large, preeminent SBx.0 series, there are several smaller dedicated meetings throughout the world, for example the SynBioBeta conference series (SynBioBeta) and the Synthetic Biology Congress (Global Engage). Additionally, alongside the conferences and meetings, there are a growing number of academic journals dedicated to synthetic biology, which provide additional 'stickiness,' adhering the community together.[53]

These increased efforts to establish synthetic biology as a defined and recognised community, alongside the influx of resources and people into the field, suggest that the synthetic biology community has further developed and cemented since Molyneux-Hodgson and Meyer wrote their piece. Indeed, the community appears to be on its way to becoming an established discipline with a delineated community of practitioners, and a coherent epistemic

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[53] For example: *ACS Synthetic Biology*, *Systems and Synthetic Biology, Current Synthetic and Systems Biology, International Journal of Systems and Synthetic Biology.*

culture or, as Leonelli and Ankeny (2015) term such a collection of conceptual and practical norms, repertoire. Arguably, however, a significant factor in the growth and strengthening of synthetic biology's developing repertoire is training, which Molyneux-Hodgson and Meyer neglect to address.

As discussed previously, synthetic biology is explicit in its desire to be seen as a hybrid discipline, not an interdisciplinary discipline, but something much more complex. An interdisciplinary discipline is generally made up of individuals who hail from various contributory disciplines and who maintain the identity of these contributory disciplines. Whereas within synthetic biology there is a desire for the discipline to be made up of synthetic biologists, individuals who are themselves interdisciplinary, having at least some skills and expertise in both biology and engineering. Kuldell expresses this desire clearly in the following excerpt:

> "despite seeming inherently interdisciplinary, synthetic biology is, in fact, not. It does not simply put biologists and engineers in adjoining offices and wait to see what fireworks erupt at the water cooler. Instead, synthetic biology is a distinct discipline that requires its practitioners to work in ways remarkably different from the work that defines any traditional niche. Biologists who come to synthetic biology must manage complexity, rather than describe and celebrate it. Engineers must build using material under evolutionary pressures. Students who enter synthetic biology perceive the promise and limitations of the emerging discipline and because they have yet to categorize themselves as either 'engineer' or 'scientist,' these students do not see the need to collaborate as much as they see the need to parse out the problems themselves and then systematically develop the skills to solve them" (2007: 1-2).

Sean Eddy argues that such a focus on interdisciplinary people rather than interdisciplinary teams is preferably and much more likely to yield scientific progress. He writes, "when I think of new fields in science that have been opened, I don't think of interdisciplinary teams combining existing skills to solve a defined problem - I think of single interdisciplinary people inventing new ways to look at the world. Focusing on interdisciplinary teams instead of interdisciplinary people reinforces standard disciplinary boundaries rather than breaking them down" (Eddy 2005: 3). Indeed, Eddy writes, while "new disciplines eventually self-organize around new problems and approaches, creating a new shared culture," what is important for the establishment of this shared culture is that it "coalesces into the next essential training regimen for the next generation of scientists." "Interdisciplinary science," he continues, "is just the embryonic stage of a new discipline" (Eddy 2005: 3). Yet, as will be discussed below, creating such a shared culture within a new discipline is not as easy as Eddy suggests.

Bridging the epistemic cultural divide

In my exploration of the epistemic cultures within synthetic biology I was drawn to the work of Helge Torgersen (2009). Torgersen's work investigated the development of genomics, questioning whether the epistemic cultural tensions she identified between the participating biologists and computer engineers could lead to the development of a new epistemic culture. However, despite their goal of forming a coherent discipline, she found that the individual participants "remained either computer engineers or biologists with their particular mindsets and approaches to science as instilled by their different intellectual formations" (Torgersen 2009: 81). This finding ultimately led Torgersen to conclude, in regards to genomics, that "[t]he multi-disciplinary bridging of the epistemic gap has not been accomplished" (2009: 81). Such a finding of tension and lack of coherence within emerging interdisciplines is not uncommon, being echoed by Sankar et al. (2007) and O'Day et al. (2001). Indeed, as these authors, and others (such as Bartlett et al. 2016; Calvert 2010b; Etkin and Elisabetsky 2005; Lewis and Bartlett 2013) have shown, the difficult, messy, conflicted process of merging disciplines, which I encountered within synthetic biology, is common to many emerging interdisciplines. Thus, despite the promise of Eddy's claims, Torgersen's findings sounded very familiar, bearing, as they do, similarities with my own observations from the Centre.

Where I found references to the 'naysayer biologist' who 'ignorantly' thinks biology is too difficult to model, Torgersen found that the engineers within genomics looked down on the way their biologist colleagues undertook research. They, like some of the engineers at the Centre, viewed the biological approach as "a sort of handicraft" while perceiving their own field to be "a technical science with a profoundly different way of thinking" (Torgersen 2009: 75-76).[54] The biologists Torgersen interviewed, like the biologists I encountered, were equally suspicious of the engineers' approach, questioning how the results the engineers produced were related to biological questions. Ultimately, Torgersen found there to be a clear division of labour within genomics, wherein "each part has its function but does not interfere with the tasks of the other" (2009: 82).

These findings are reminiscent of both the epistemic cultural clashes Keller (2002) identified (though she does not identify them as such) as instrumental in the failure of past attempts to integrate an engineering approach into biology, and my own findings from within the Centre. Initially the parallels between Torgersen's findings and my own led me to question whether the epistemic gap within synthetic biology was likewise too wide to be easily bridged, and thus the internal differences too fundamental for a coherent discipline to form. Indeed, even though those within the Centre were eager for synthetic biology to succeed as a hybrid discipline, and appreciated the role played by those from both biology and engineering, some were uncertain how exactly this could be achieved.

During a conversation at the lab bench, Maria,[55] in what seemed to be a clear description of synthetic biology's epistemic cultural divide, insisted that while biologists and engineers can learn each other's techniques and methods,

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[54] This bears a striking resemblance to the attitudes expressed by several members of the Centre, which are discussed in chapter four.

[55] A Masters student with a background in biochemistry.

they cannot so easily learn their way of thinking. She told me, "*biologists and engineers have very different ways of looking at things, different perspectives, different ways of thinking, different languages, and while they can appreciate each other's approach, they don't really ever get into the mode of thinking of the other*." "*Biologists*," she explained, "*can't reach the extra level of engineers' thinking, and engineers can't reach the extra level of biologists' thinking. Ultimately they can't fully see things from the other's perspective, they can't engage in the 'abstract thinking' of the other.*" Consequently, Maria concluded that the best she believes synthetic biology can hope for is collaboration, not "*true hybrid synthetic biologists*" (that is synthetic biologists who are fully trained as both engineers and biologists).

Maria justified this perspective by claiming that "*people naturally tend towards one way of thinking or the other, and this cannot easily be taught. Even if you train people in both* [disciplines] *at the Masters level they will tend towards one or the other perspective*."[56] Thus Maria maintained that having an understanding of each other's perspective, and an ability to speak each other's language is important to foster collaboration but it won't produce "*hybrid*" workers. Furthermore, Maria stressed that she doesn't believe that such dual training "*would be of benefit anyway as if people really do get an equal training in each, their knowledge of both would be superficial and they would not be able to engage in the abstract thinking of either*." Ultimately then, Maria fears that attempts to create interdisciplinary individuals, of the type Eddy (2005) promotes, will result in a generation of synthetic biologists who are Jacks of all trades, but masters of none.

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[56] This is rather a big claim from Maria, and it is one I cannot find literature to substantiate so I will not attempt to do so. I did indeed find that the members of the Centre, even those who were currently being, or had been, trained at Masters level in both engineering and biology, did tend towards one way of thinking or the other. However, this may well be due to their undergraduate and secondary school training specializing in one field or the other, rather than due to some innate tendency. As discussed above, Knorr Cetina (1999) asserts that epistemic cultural divisions are deeply entrenched in all levels of education. With students being taught to prioritise certain goals, ask certain questions, and speak in certain ways, all of which differ between disciplines, and thus between epistemic cultures.

If one were to solely judge by Maria's adamant assertions about the prospects of producing hybrid synthetic biologists, then it would seem like the epistemic cultural divide between biologists and engineers within synthetic biology is too wide to easily bridge and that attempts to do so would compromise the success of the discipline. However, as I shall discuss below, I observed two distinct strategies adopted by members of the Centre determined to overcome the difficulties Maria addressed and ultimately bridge this divide. The first of which was the embracing of close, respectful collaboration.

Close collaboration

Like Maria, Stephanie was also adamant that the best synthetic biology can and should hope for is respectful collaboration between biologists and engineers, rather than individuals who possess all of the knowledge and skills of both sides of the discipline. She asserted that, while the discipline of synthetic biology is a hybrid, the synthetic biologists themselves are not, and she does not believe it would be beneficial to make them so. To try and teach synthetic biology as a hybrid discipline (part engineering and part biology) to undergraduates would, Stephanie claimed, result in students with "*a superficial understanding of both disciplines, but not enough depth of knowledge in either*," a claim that echoed Maria's concerns. Thus Stephanie believes the University[57] is correct in only offering degrees in synthetic biology, as an integrated course, at postgraduate level, once, that is, "*the students already have a good grounding in a sole discipline*" (Stephanie, senior researcher, engineering).

There is sense in Stephanie's argument, a support for depth rather than breadth of training. However, I cannot help wondering if this singular early training is, at least in part, the cause of the difficulties Maria claimed synthetic biologists have engaging in the abstract thinking of the other side of the discipline. Would they be better able to engage in "*the mode of thinking of the*

[57] 'The University' here refers to the university where the Centre was located.

other" if they had a broader undergraduate training? But if they did, would this be, as Stephanie and Maria claim, at the expense of their ability to work at the forefront of either discipline and thus be a detriment to synthetic biology? As there are currently no undergraduate degrees in synthetic biology, it is not yet possible to answer this question, but it is one that the discipline is going to have to confront as decisions are made about the best way of training future synthetic biologists. Given that Stephanie supports the University's current system, where synthetic biology is taught only at postgraduate level,[58] she argued that "*it shouldn't be about producing synthetic biologists who can do the biology and the engineering themselves, but rather about producing biologists and engineers with an appreciation for what they can gain from working together*." It was this type of collaboration that she engaged in herself, primarily with Janet.

As a result of their commitment to respectful partnership Stephanie and Janet are ultimately the prime example of collaboration within the Centre. These two women have enough experience in, and knowledge of, each other's discipline to be able to work closely and respectfully. They understand the potential and the limitations of the other's input, and above all else, they are willing to compromise and adapt to work in with the other. However, not to the extent that they become a consultant on the other's project rather than a collaborator on a joint project. Ultimately then it is through such close, respectful collaboration that they, and others like them, are attempting to bridge synthetic biology's epistemic divide. They view themselves as having different strengths, different skills, and different approaches from each other and they do not believe that they can individually embody both sides of synthetic biology. Thus, by banding together in collaboration, they can each embody half of the discipline and together they can produce the desired hybrid work. Here Stephanie explains this approach to collaboration, and why

[58] With the exception of a single undergraduate course which students from both biology and engineering sub-disciplines can take as part of their separate degrees.

she views the engagement of those higher up in synthetic biology in such collaboration as important.

> *It's not enough to sort of have a joint student and for the student to become, if you like, the new generation of synthetic biologists, to represent what synthetic biology is about. It's not enough to bring the supervisors closer together, because you can have the student going to one and being told about maths and non-linear dynamics*[59] *and going to the other and being told about Western blotting and qPCR.*[60] *So, inevitably if people higher up don't start making an effort then it's not going to work out. So that's why I'm always sceptical about joint projects because unless you make an effort it's not going to be fruitful. But . . . if you're going to start a collaboration I think you need to start with something that both people can contribute to, otherwise you're not going to have the commitment from both. One is just going to be an advisor of some sort.*
> (Stephanie, senior researcher, engineering)

In this way Stephanie explained both the approach to collaboration she and Janet take, an approach that sees them developing projects together and working on them as equal partners, albeit in their separate locations, and also her belief that synthetic biology cannot, and will not, work if it is solely reliant on the next generation. As she states above, the supervisors, in other words the more senior participants in synthetic biology, also need to be committed to collaboration, to understanding each other and working together. That is, they also need to be committed to bridging the divide. For Stephanie, a central aspect of her belief that synthetic biology needs to embrace collaboration between those with different areas of expertise, is her concern, reminiscent of

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[59] Non-linear dynamics is the study of systems governed by equations in which a small change in one variable can induce a large systematic change. The discipline is more popularly known as chaos theory.

[60] Western blotting is an analytical technique used to detect certain proteins in a tissue sample or cell culture. qPCR stands for quantitative polymerase chain reaction, which is a methodology for studying gene expression.

Maria's, that training everyone in both biology and engineering will not yield synthetic biologists with enough skill in either to drive the discipline forward.

However, to look at this another way, those within the Centre, such as Stephanie, who had received the entirety of their training in one of synthetic biology's parent disciplines, rather than in synthetic biology itself, find themselves in a challenging position. They are trying to embrace the discipline's hybridity, but without the training to be able to perform all the necessary tasks themselves. Yet, from my conversations with those within the Centre who fit this description, it would seem that these same individuals are keen to avoid the kind of conflict and division Torgersen identified within genomics. To this end, these, largely senior, members of the Centre were attempting, as Janet and Stephanie were, to forge close, respectful collaborative relationships. While this is arguably a valid and potentially productive approach to their work, it is also, arguably, the only approach open to them, unless they wish to retrain or leave the discipline.

Stephanie may well be right that to train everyone in both biology and engineering would not produce interdisciplinary individuals capable of driving the discipline forward. However, should she believe that this was the only way of driving the discipline forward, or that training in both was essential, she would, given that she is only trained in engineering, be simultaneously excluding herself, and the vast majority of the senior figures in synthetic biology (who likewise are only trained in one of the 'sides' of synthetic biology), from having an important role in the discipline's success. I do not wish to suggest that interdisciplinary training is essential, nor that close collaboration cannot yield success, but rather I wish to highlight that it is perhaps not surprising to hear such views from senior members of the discipline, and that such adamant claims that interdisciplinary individuals cannot and will not succeed may be driven, at least in part, by self-interest.

Furthermore, while Stephanie and Janet's working relationship is clearly a model example of such collaboration, the reality did not always match this ideal. Despite every member of the Centre at some point espousing to me the benefits of collaboration, I also witnessed tensions between the two 'sides' of such collaborations, albeit usually surreptitious (eye-rolling during meetings for example) or divulged in private (such as vented frustrations and name-calling). These tensions were often the result of frustrations with the perceived ignorance or arrogance of those on the other 'side.' However in a few cases, a belief in the superiority of his or her own half of the collaboration saw some individuals within the Centre unwilling to be flexible or to compromise within their collaborations. Sara, for example, told me of her experiences with Philip (senior researcher, engineering) who was steadfastly unprepared to compromise on his models:

> *He would always say, 'This is what I want, and nothing else!'* [Laughs] *'I want this, this, and this. That's it, come back to me with that.'*
>
> (Sara, doctoral student, biology)

Such tensions in interdisciplinary relationships are common,[61] and can stifle collaboration. However rather than avoiding collaboration, there was a clear desire within the Centre to compromise. Anna described the importance of this commitment while also acknowledging the difficulty of enacting it.

> *You might have these great skills but then if . . . you can't merge them together then what's the point of being in the same centre? So . . . everyone needs to think more . . . think of it from a modeller's*[62] *point of view and think of it from a biological point of view. That's a difficult thing . . . at the initial stages I think that everyone wants to work together but you need to learn to gel . . . and actually compromise a bit.*
>
> (Anna, doctoral student, biology)

For some the solution to such tension was indeed to compromise and, according to Grant, trust more.

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[61] See for example Lélé and Norgaard (2005).

[62] Given the prevalence of modelling within the work of the 'engineers' in synthetic biology, they were often referred to as 'modellers' even though they do not necessarily self-identify as such.

If biologists come to me and say, 'OK, we would need a tool to analyse those data and to represent them in a particular way,' it will take me time to develop it and I will probably not see the immediate benefit scientifically speaking for the work I do now, but there will be probably benefit in the long-run. So investing time and energy in developing things that are not directly, immediately . . . of particular use for you, requires some trust relationship.

(Grant, senior researcher, engineering)

Such a commitment to collaboration, in the absence of immediately personal benefit, may have been driven by another key component in successful collaborative relationships, a component that Peter described as, a willingness "*to step outside of their comfort zone and to listen and to try and understand the other perspective*" (Peter, senior researcher, biology). This willingness to understand the other perspective came up repeatedly in the descriptions I was given of positive collaborative relationships. However it also arose as a motivator for some within the Centre to move beyond collaborative relationships and towards the academic self-sufficiency of becoming interdisciplinary individuals.

Interdisciplinary individuals

The importance Eddy places on the training of the next generation of scientists, so that they may become the interdisciplinary individuals necessary for the emergence of a new discipline, got me thinking about the role of training in the development of a coherent epistemic culture for synthetic biology, and thus the students within the Centre. In the last couple of years, students have started emerging from the university, where the Centre is located, with masters and doctoral degrees in synthetic biology. Given the requirements that all synthetic biology students incorporate elements from both biology and engineering into their projects, these graduates may, despite Stephanie and Maria's misgivings, be some of the first examples of synthetic biology's trained interdisciplinary individuals. However the degree to which students within the Centre embraced this interdisciplinarity differed. Some were keen to maintain the academic identity of their undergraduate discipline, possibly because this felt more secure,[63] while others were eager to shed such an identity in favour of calling themselves synthetic biologists.

Adopting such an interdisciplinary approach to their work may well feel risky but, as Zerubavel writes, it is also a potential route to innovation. "Creativity," he asserts, "usually involves defying existing divisions and integrating mental realms and domains that are traditionally perceived as distinct and separate from one another" (Zerubavel 1995: 1098). Furthermore, I would argue that those who eagerly embraced their interdisciplinary training were, like those who pursued close, respectful collaborations, finding a way to bridge synthetic biology's epistemic cultural divide. For, as Knorr Cetina makes clear, education plays a significant role in the development of epistemic cultures. Thus, where separate training has yielded two distinct academic communities within synthetic biology, as Malcolm[64] acknowledged in the first half of this chapter a well-balanced, interdisciplinary synthetic biology education could not only provide students with a broad knowledge base and a fluency in both languages, but also teach them to balance the goals and research interests of both sides of the endeavour. Ultimately then, such an education would be instrumental in the emergence of a hybrid epistemic culture for synthetic biology. While I would not currently go so far as to say such a culture exists, given the emphasis Knorr Cetina (1999) places on the role of education in the formation of epistemic cultures, it is certainly a potential outcome as more and more synthetic biologists emerge from dedicated training courses.

In considering who at the Centre best embodied Eddy's notion of interdisciplinary individuals, four doctoral students in particular came to

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[63] There is arguably a certain security provided by an established academic identity, such as being a mechanical engineer or a biochemist, that is missing when one identifies as belonging to a discipline many have never heard of. Indeed, despite promoting the notion of having a "flexible mind" when considering the boundaries of disciplines, Zerubavel (1995) notes that it can be difficult to occupy an academic grey area, especially when encountering those with, what he terms, "rigid minds."

[64] One of the Centre's directors.

mind. Two of whom had come to synthetic biology from biology and two from engineering. These four, Lewis, David, Simon, and Trevor,[65] all specifically expressed a desire to overcome the division between biology and engineering in their own work by incorporating equal amounts of both sides of synthetic biology into their projects, a desire they worked hard to put into practice. They all read widely on both sides of the divide and saw themselves as intellectually and practically inhabiting the whole, rather than half, of the discipline. However, despite their enthusiasm such individuals are, as yet, the minority within synthetic biology and they are a minority located exclusively in the lower tiers of the discipline, as students and postdocs. As such, they encountered some resistance and difficulty as they strove to achieve the desired hybridity.

Lewis, who frequently spoke of his wish to embody the hybridity synthetic biology is aiming to achieve, despite often struggling to do so, proves a useful case study to explore the challenges facing these budding interdisciplinary individuals. As previously addressed, Lewis struggled against what he termed the "*academic arrogance*" of his supervisors. According to Lewis, his supervisors, a biologist and an engineer by training, saw their own discipline as providing the central component to his project, while Lewis himself wanted to find an equal balance between the two. He stated that the main difficulty he was encountered in achieving this balance was his supervisors' biases, as each had a different idea about where the project was headed. To demonstrate this point Lewis drew me a picture in the air, saying that he and his supervisors were currently standing relatively close together, but that Grant sees the project angling off to the left towards modelling, and Martin sees it angling off to the right towards biology, while Lewis is aiming for a straight path between the two. Yet, despite finding it difficult to strike this balance and keep the project on track, Lewis went on to say that he is determined to hold this line

[65] These four are, like the vast majority of the members of the Centre, all male. When I first started my fieldwork there was only one female doctoral student at the Centre, though by the time I left there were three.

as he fears that, if he doesn't, his project could end up thinly spread across the entire spectrum of synthetic biology, from engineering to biology, without integrating them into something more coherent.

To Lewis' mind, lots of collaborations in synthetic biology do not manage to retain the benefits of both contributing arms of the discipline. Again

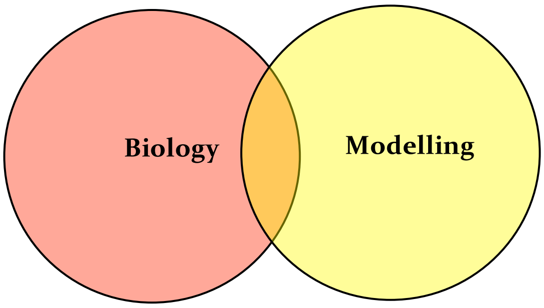

Figure 3: Lewis' Venn diagram of the overlap between biology and modelling in relation to synthetic biology collaborations

describing a situation in terms of a diagram, Lewis drew me a Venn diagram in the air, saying that some collaborations only manage to capture the small area where biology and engineering, or as he termed this half of synthetic biology "*modelling*," overlap or are more compatible and in so doing miss the real richness and value that each brings to the table. His diagram, if noted down, would have looked something like this:

Lewis believes that people settle for this form of collaboration, as it is much easier to achieve than actually bringing the two disciplines together in a more complete way. "*Many synthetic biology projects,*" Lewis contends, "*are simply biology projects with a bit of modelling tacked on, or modelling projects that do a little bit of wet-lab work to test feasibility*." That is, they include either, the red and the orange in figure 3, or the yellow and the orange, but seldom all three areas as Lewis intended to.

This, it must be noted, is not the kind of collaboration Janet and Stephanie engage in, and indeed is exactly the kind of situation they are determined to avoid. However, if this asymmetry is indeed the norm, as Lewis suggests, this may help to explain why Lewis encountered the resistance and misunderstanding that he did from his supervisors. They may well expect him to produce a synthetic biology project that incorporates their own area of interest, and the area of cross over with the other side, but little beyond that. Or they may be so unfamiliar with the demands and potential of the other side of the discipline that they, while eager to encompass all that synthetic biology has to offer, do not fully appreciate what this would entail. I cannot determine which, if indeed either, of these theories is more accurate as, given that Lewis spoke to me in confidence, I did not question either of his supervisors about this.

Yet, despite the difficulties Lewis faced pursuing his goal of becoming an interdisciplinary individual, both in terms of resistance from his supervisors, and indeed the larger hurdle of having had to learn biology, and laboratory practices, for the first time as a Masters student, Lewis never opted for the easier option of pursing collaboration over personal hybridity. Rather, and inadvertently in line with Eddy's position on the matter, Lewis commented that he believes it is better and more successful when the hybridity of synthetic biology is embodied within a single person, a belief that ultimately fuelled his determination.

Nevertheless, despite the emphasis Eddy places on training, it is not only students like Lewis who can become interdisciplinary individuals. Calvert (2010b) suggests that some participants in interdisciplines can shift from engaging in collaborative interdisciplinarity to becoming interdisciplinary individuals themselves as they gain experience, skills, and knowledge from across the discipline. Pam Silver, a senior synthetic biologist at Harvard, for example wrote, "I come to synthetic biology as one of the biologists . . . But having worked in the field of synthetic biology for the last few years, my thinking has evolved somewhat from a biologist's perspective to an engineer's approach" (Silver 2009: 283). Suggesting that with both time and experience, even senior participants within the field, such as Silver, can and are beginning to have a much more interdisciplinary perspective on their work.

Eddy asserts that, "[p]rogress is driven by new scientific questions, which demand new ways of thinking. You want to go where a question takes you, not where your training left you" (Eddy 2005: 3). As such, it is not necessarily a hindrance that most of the current participants in synthetic biology were not trained in synthetic biology, but rather in branches of biology or engineering. For, to follow Eddy's line of argument, even though these parent disciplines have strong epistemic cultures that differ from each other in significant and at times conflicting ways, if the individuals are committed to following where the questions take them into the realms of each other's disciplines, to break down the epistemic cultural divides, a new science will emerge, and its participants, regardless of their training, will become interdisciplinary individuals.

As such, synthetic biology may be driven forward by both newly trained interdisciplinary individuals, and those from differing disciplines who are committed to exploring new and challenging questions in new ways, through close, respectful collaboration. Indeed, rather than seeing such collaborations as the best that can be achieved if we want to ensure that a high degree of expertise in both biology and engineering is fed into synthetic biology, there is an argument that having participants with differing perspectives should be seen as a positive; a strength rather than a weakness or an unfortunate reality. Interestingly it was Lewis who first put this argument to me.

Explanatory pluralism

Despite his personal commitment to becoming an interdisciplinary individual, and his belief that hybridity is better embodied in one person than two, Lewis did not believe that synthetic biology would benefit from everyone sharing the same perspective on the discipline. Rather, he questioned the notion that in order to succeed, such uniformity within synthetic biology was required, arguing instead that the idea of everyone sharing a perspective, and thus asking the same sorts of questions, was a potential problem for the discipline. Admittedly Lewis believes that synthetic biology should ultimately aim for a united perspective in the future, however as he saw it such a united perspective would not be a narrow perspective, but rather would encompass all of the explanatory tools of the currently contributing perspectives. As I sat and listened to Lewis speak of the benefits of the differing perspectives within synthetic biology, the concept of explanatory pluralism came to mind.

De Vreese et al (2010) explore the role of explanatory pluralism in the medical sciences, contending that the explanatory practices of scientists show how their different epistemic interests can lead them to choose different forms of explanation at different levels. They argue that a combination of such explanations gives a much more holistic response to a question than any of the single, contributing explanations could. As such, they define explanatory pluralism as "the view that the best form and level of explanation depends on the kind of question one seeks to answer by the explanation and that one needs more than one form and level of explanation to answer all questions in the best way possible" (De Vreese et al. 2010: 372). Evelyn Fox Keller goes further writing, in regards to the field of biological development, that after exploring "the de facto multiplicity of explanatory styles in scientific practice" and the "diversity of epistemological goals which researchers bring to their task," (2002: 300), she has come to believe that such diversity may well be a requirement in investigating this inherently complex field. Thus she suggests that explanatory pluralism "is now not simply a reflection of differences in epistemological cultures but a positive virtue in itself, representing our best chance of coming to terms with the world around us" (2002: 300).

Synthetic biology is arguably an equally complex field, consisting as it does of individuals who hail from differing epistemic cultures. Thus it seems plausible that, as those within the discipline seek to come to terms with its limitations, its capabilities, and its potential promise for the future of biotechnology, it would similarly benefit from explanatory pluralism. I put this idea to Lewis who, not only agreed, but also illustrated his agreement with another of his fantastic verbal diagrams. Lewis stated that, to his mind, synthetic biology is really a hybrid discipline as a whole but, if you zoom in, it is made up of lots of heterogeneous, rather than homogeneous, researchers. As such, he said, "*synthetic biologists are like the colours red and yellow*" (meaning that biologists are one colour and engineers the other), and:

> *"in forming the discipline of synthetic biology they do not mix together so that everyone becomes orange, but rather stay as dots of*

red and yellow. However, from a distance, and because of the way the dots are situated close together, they appear as a whole to be orange. Thus it is through the collaboration of the two groups that you get something new, but they still maintain their different perspectives individually."

(Lewis, doctoral student, engineering)

Surprisingly, despite his determination that synthetic biologists should ultimately become self-reliant interdisciplinary individuals, Lewis has hailed here the role of collaborations such as Stephanie and Janet's. Indeed, like Stephanie, Lewis concluded that the most important things for the success of the discipline are communication and respect for each other's perspectives and expertise.

Jessica, a doctoral student with a biological background, also spoke of the benefits of explanatory pluralism. During our interview, and while speaking of the way biologists and engineers work together within the Centre, Jessica said:

"So for me, in a way, it's been a very positive change where I've been made aware that I can do more than I previously thought, and that kind of goes back to what's good about putting engineers and biologists together, you suddenly realise there's more ways of answering the questions, and I've sort of realised that for myself personally as well."

(Jessica, doctoral student, biology)

Thus Jessica not only saw the benefits of having different people with different perspectives attempting to answer research questions, but she was also learning to challenge her own approach to questions and hence attempt to apply the approach of her engineering colleagues to her own work. This quote from Jessica reminded me of a quote from microbiologist and biophysicist Carl Woese regarding physics and biology. Woese railed against the all too common notion that the relationship between these sciences was one of hierarchy, contending instead that it should be viewed as one of reciprocity. As such, he wrote, "both physics and biology are primary windows on the world; they see the same gem but different facets thereof (and so inform one another)" (Woese 2004: 185). In striving to view as many facets of the 'gem' of synthetic biology as she can, Jessica, like Lewis, can be seen as both an advocate of explanatory pluralism and an emerging interdisciplinary individual herself.

As Rheinberger writes, and as I believe these quotes from Lewis and Jessica indicate, such inconsistencies in individual synthetic biologists' epistemic cultures, in, that is, their knowledge and approach to the field, are not necessarily impediments to the discipline's progress. Rheinberger, in his 1997 book, *Towards a History of Epistemic Things: Synthesizing Proteins in the Test Tube*, writes, "[r]ecombination and reshuffling, bifurcation and hybridization within and between experimental systems, are prerequisites for producing unprecedented events. Such events could not happen if the lines of descent were bred too 'pure'" (1997: 184-85).

This clearly fits with Keller's notion that explanatory pluralism is of benefit in understanding the world, but it also fits with Eddy's notion that progress is driven by an interdisciplinary rather than a singular disciplinary approach. Eddy, as discussed above, contends that such progress is best pursued by interdisciplinary individuals, but as Rheinberger (1997), Keller (2002), Lewis, Stephanie, and Jessica assert, close and respectful collaboration can also produce the desired unprecedented events that drive a new discipline forward. Ultimately, both strategies to overcome the discipline's epistemic cultural divides (close, respectful collaborations and learning to become interdisciplinary individuals) stem from the same desire: to embrace all that biology and engineering can offer synthetic biology. Furthermore, these strategies are key factors in the effort to establish synthetic biology as a clear, coherent, and well-defined discipline in its own right. Thus it would seem that synthetic biology, as it currently stands, is being held together and driven forward by, using Lewis' analogy, a sea of closely situated red and yellow dots, with a growing number of orange, interdisciplinary individuals among them.

A metaphor for synthetic biology's interdisciplinarity

Lewis' analogy of interdisciplinary collaboration being like differently coloured interacting, and merging, dots not only helped me to make sense of the interdisciplinary interactions which are driving the emergence of synthetic biology, but it did so by bringing to mind images of intercellular interactions. Clearly my years of sitting through biology, biochemistry, and genetics lectures have had a lasting impact on my conceptual image banks. Yet, the more I thought about this, the more intercellular interactions came to make sense as an analogy for the type of interdisciplinarity I was observing within synthetic biology, and how it contrasted with the type of interdisciplinarity I was reading so much about in the literature.

Indeed, many of the accounts of interdisciplinarity in the literature discuss cases where the internal disciplinary boundaries remain clear but where lines of communication and cooperation are opened between them. Such examples are primarily interdisciplinary research networks rather than new disciplines (see for example Boix Mansilla et al. 2016). There are some new disciplines amongst them (see for example A. Clarke 1998; Etkin and Elisabetsky 2005) however these seem to be interdisciplinary disciplines which maintain clear, internal, divisions. This kind of interdisciplinarity is, I believe, analogous to the kind of intercellular interactions that occur within the immune system.

Within the immune system there are situations whereby two or more different types of cells interact, and arguably collaborate, with each other on a common problem. Yet, despite their close interactions, these contributing cells ultimately remain distinct and independent from each other. Figure 4 displays an example of this kind of intercellular interaction with three different cells (a dendritic cell, T helper cell [Helper CD4+ T cell], and killer T cell [Cytotoxic CD8+ T cell]), interacting to deal with the unwelcome antigen material.[66]

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[66] Within the immune system many cell types, including T cells, B cells (both types of lymphocytes), and dendritic cells (a variety of antigen-presenting cell) interact. These three cell types, for example, interact in the lymph nodes to initiate and shape the adaptive immune response, yet they nevertheless remain distinct from each other.

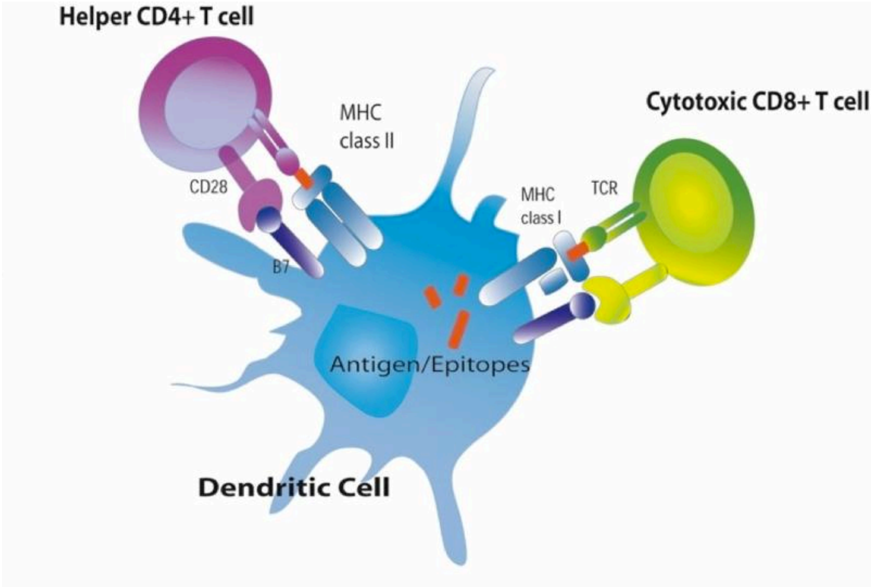

Figure 4: Intercellular Interactions in the Immune System (Boston University School of Public Health)

I would argue that the subworlds of the reproductive sciences Clarke (1998) explored interact similarly. These subworlds fit within the world of the reproductive sciences like the various cells fit within the immune system. They interact, communicate, and cooperate with each other as they address issues and factors of reproduction, but they remain separate and distinct from each other. Much like the cells of the immune system interact, communicate, and cooperate with each other in response to antigens, but remain distinguishably different cells throughout the process. By contrast, interdisciplines such as neuroscience (Swazey 1992) and physics (Kuhn 1962), which engage interdisciplinary collaboration as a step towards the formation of new, cohesive, disciplines, employ a different form of interdisciplinarity, a form which lends itself to a different cellular analogy.

This second form of interdisciplinary, I would argue, is analogous to cell fusion, a process by which different types of cells merge together to form a new hybrid organism, or cell line. In such a situation the merging cells fuse their cellular walls (their external boundaries), and often, eventually, also their nuclei (their bounded, DNA-containing cores), thus producing a new kind of hybrid cell. The stages of such a merger of cells are shown in figure 5.

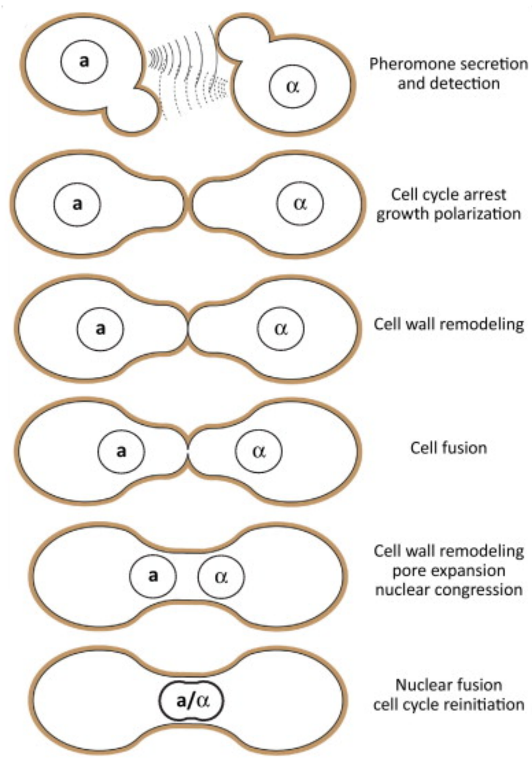

Figure 5: Heterotypic Cell Fusion (Aguilar et al. 2013)

The parent disciplines in this model of interdisciplinarity, like the cells in this figure, start out with distinct, separate identities. They then become attracted to each other, in cells due to pheromones and in interdisciplinarity due to the knowledge and/or materials the other can provide them. They move closer to each other, begin to interact, and, professionally speaking, bind themselves together forming a new disciplinary boundary which encompasses them all, like a new cell wall. However, for a time, this new singular discipline, or cell, is not internally cohesive, but rather maintains the disciplinary identities, or nuclei, of the parent disciplines or cells. Until, that is, these too merge in nuclear fusion, thus creating a hybrid discipline, like a new kind of cell, which contains elements from its parents but is now clearly distinct from them.

Disciplines which started out as 'interdisciplines,' if you will, such as physics, and biochemistry, have arguably completed this process. That is, they have merged their constituent nuclei (mathematics and natural philosophy in the case of physics, and biology and chemistry in the case of biochemistry) to become like the synkaryon (Aguilar et al. 2013) depicted in the final step in figure 5, a completely hybrid entity. Whereas genomics, as Torgersen depicted it in 2009, and as discussed above, had not achieved this status. Despite the existence of a disciplinary 'cellular wall,' Torgersen describes genomics as being internally divided, perhaps like the heterokaryon (Aguilar et al. 2013) depicted in the second to last step of figure 5, a cell that is, with two or more separate nuclei within it that may, or may not, merge. That is, there were two or more disciplinary identities, and thus epistemic cultures, within genomics, rather than one.

It must however be stressed that such disciplinary merging, as that which physics and biochemistry have undergone, does not produce a uniformly coherent discipline with all adherents ascribing to the exact same theories, methods, and approaches to their work. Rather the key word here is hybrid. Arguably all disciplines, regardless of their process of formation, are internally hybrid. Uniting as they do individuals with widely varying approaches to their common field of inquiry. Such divergent strands of research within a discipline are entirely normal. Yet, I would contend that such divergent strands maintain enough common ground, as well as enough of a common identity, to remain strands of the same disciplinary bow. Thus despite such internal differences, each discipline, as Knorr Cetina (1999) stresses, maintains its own epistemic culture, with its own set of practices and arrangements which shape the epistemic machinery of those within the discipline. Thus the result of disciplinary nuclear fusion is, I would argue, a new hybrid epistemic culture. Not a uniform stream of automaton-like scientists 'doing' that discipline in the exact same way, but rather a group with enough common ground to tie them together.

Thus in terms of synthetic biology, I would argue that, like Torgersen's description of genomics, it is similarly a discipline that is poised between having two distinct, conflicting, yet interacting, internal epistemic cultures, and having a singular, but hybrid, epistemic culture. As an emerging hybrid discipline it has a shared disciplinary boundary, its 'cell wall,' and it is working towards a universal sharing of disciplinary components such as language, methods, research objects, and knowledge base. Even though different individuals will undoubtedly apply such common epistemic machinery very differently. Yet, as discussed above there remains enough tension and division between the discipline's two 'sides,' or epistemic cultures, that I would argue that synthetic biology has not yet reached this point. It has not yet undergone the disciplinary equivalent of nuclear fusion, the merging of its epistemic cultures into a hybrid epistemic culture, and as such is currently more like a heterokaryon than a synkaryon. Thus, I would contend, that synthetic biology is currently occupying a grey zone on the path of interdisciplinarity, a boundary spanning zone between being two distinct disciplines and being one hybrid discipline.

Conclusion

As laid out above, the hybrid discipline of synthetic biology is the site of conflict and compromise. Synthetic biology is a young discipline that is drawing participants from two very different academic realms, biology and engineering. These participants are determined to see their fledging discipline succeed, however in order to make this happen they are having to negotiate and overcome many challenges, including differences in: language use, knowledge base, methods, research questions, research objects, and general approach to research and data. I have argued above that these disparities are due to epistemic cultural differences, and that the cluster of differences I identify not only highlight the negative side of epistemic cultures, but that such epistemic cultural differences may be implicated as obstacles to other attempts at interdisciplinarity, both future and past. For, as Keller (2002) so clearly addresses, biology and engineering have never been easy bedfellows, with several significant attempts to bring them together having failed, at least in part, because of such disciplinary differences.

Thus it is, as I outlined in the first half of this chapter, biology and engineering are not easy bedfellows within synthetic biology either. For, despite public protestations that biology and engineering are being brought together through a process of unproblematic and systematic assimilation, as I have discussed above the reality within the Centre was quite different. Tensions and frustrations were regularly in evidence as those within the Centre toiled to achieve the desired disciplinary hybridity. However despite these difficulties, the discipline continues to grow and strengthen, a process of emergence that can be tracked using Molyneux-Hodgson and Meyer's notion of movement and stickiness (2009). Indeed, with its continual influx of people and resources and the growing number of journals, conferences, and courses dedicated to the subject, synthetic biology appears to be moving further towards success than its predecessors. This progress, I have argued, is at least partly due to the dedication of those involved, who, in their different ways, are attempting to overcome the epistemic cultural barriers between synthetic biology's parent disciplines, biology and engineering.

Some, especially those in more senior positions who were trained entirely in one of these disciplines, rather than in synthetic biology itself, are, like Stephanie and Janet, attempting to overcome these barriers and undertake truly hybrid projects through the formation of close, respectful, collaborative working relationships. Those working in this way are, through necessity, learning the language, methods, approaches, potentials, and limitations of the other side of the discipline, and thus it is possible that they may find themselves, as Pam Silver and Jessica did, adopting a more hybrid approach to their own work as a result. Others, especially those like Lewis who are still undertaking their academic training, have opted for a different approach to overcoming the epistemic cultural separation between synthetic biology's two 'sides.' Rather than engaging in close collaboration with those from the other ‘side,’ they are instead attempting to straddle the divide themselves, by not only learning the theory of the other side, but also the practice so that they can undertake both the lab work and the modelling work themselves.

Such a commitment to becoming hybrid not only suggests that these synthetic biologists will emerge from their training as interdisciplinary individuals (Eddy 2005), but also that they may, with their knowledge of, and familiarity with, the epistemic cultures of both parent disciplines, be instrumental in forging a new hybrid epistemic culture for synthetic biology. An epistemic culture that incorporates not only the hybrid language of synthetic biology but also the languages of biology and engineering, the wide-ranging lab and computer-based practices of synthetic biologists, and an understanding of the needs, timelines, and limitations of the whole of the endeavour, and not just half of it.

While this exploration of synthetic biology reveals more complexity than the claim that, it is simply, and uncomplicatedly, a hybrid discipline, would suggest, it is, I maintain, a more accurate depiction of what happens behind closed doors. Given that the senior members of the discipline are, by and large, trained in only one side of the discipline, this mixed approach to achieving the discipline’s desired outcome of hybridity, seems to be what is driving the discipline forward. As it allows the senior members to contribute and lead the discipline, as a whole, through close collaboration and an appreciation for explanatory pluralism, while the next generation gain sufficient experience, training, and perspective in synthetic biology as a hybrid discipline. Whether this next generation of interdisciplinary individuals come to dominate synthetic biology, and whether, through their bridging of synthetic biology’s dual contributing epistemic cultures, they forge a fully-fledged hybrid epistemic culture for the discipline, remains to be seen.

Yet, the challenges of undertaking such a merging of the contributing disciplines’ epistemic cultures, of their practical and conceptual norms, may be, I contend, simply par for the course in the formation of a new, coherent, hybridised interdiscipline. As two, or more, disciplines strive to create a new hybrid discipline at their intersection, rather than just a collaborative research network of contributing disciplines, they undergo a process of disciplinary merging which, I contend, bears similarities to that of cells undergoing cell fusion. A process whereby a disciplinary boundary is first formed, and then, within this boundary, the contributing disciplines begin to increasingly share components to such a degree that, should a complete merger occur, their disciplinary nuclei, or epistemic cultures, fully fuse, establishing the academic entity as a new cohesive hybrid discipline.

While synthetic biology needs to mature more before we will see if such a coherent epistemic culture does fully emerge for the discipline as a whole, synthetic biology's interdisciplinary individuals, both those who are newly trained and those in senior positions, do, through their commitment to hybridity and to going where the question takes them and not where their training left them, appear to be moving the discipline towards this final step of fusion. However, in the meantime, I suggest that synthetic biology is moving through a interdisciplinary grey zone, being no longer made up of two distinct disciplines, but not yet being the hallowed single, hybrid discipline either.

Chapter Four: Engineering Biology

Following the work of Karin Knorr Cetina (1999), each discipline can be thought of as having its own epistemic culture. The distinct collection of practices, beliefs, arrangements, and mechanisms, which shape both the knowledge claims of a particular discipline and determine how those within it come to know what they know. Knorr Cetina (1999) developed the concept of epistemic cultures in order to both challenge the notion of scientific unity, and to explain the differences she encountered between two branches of science, molecular biology and experimental high energy physics. However, while Knorr Cetina (1991, 1999) discussed the ensemble of elements which she believes constitute an epistemic culture, the mundane practices and concepts that shape such things as the language and methods used, the way research entities are engaged with, and the methods of collaboration, she did not explore the process by which such practical and conceptual norms are developed. However as discussed in chapter three, within synthetic biology it was just such a process of discipline, and thus epistemic culture, formation that I encountered.

Synthetic biology, as explored in the previous chapter, is an emerging discipline located at the intersection of biology and engineering. An emerging discipline striving to hybridise its constituent halves and yet struggling with, what I argue are, their epistemic cultural differences. Yet despite these differences, I conclude in chapter three that synthetic biology is immersed in the process of disciplinary formation. Having moved beyond being two separate disciplines but not yet having reached the point of being one coherent discipline. This lack of coherency, I contend, is due to the lingering epistemic cultural divide at the discipline's centre. A divide that is being bridged by interdisciplinary collaboration, and interdisciplinary individuals, both of which are, I would argue, establishing new practical and conceptual norms for synthetic biology. Practical and conceptual norms which are founded in their interdisciplinary work, and which are slowly but surely establishing a coherent, and distinct hybrid epistemic culture for synthetic biology. It is the work to establish this hybrid epistemic culture that I turn to now drawing on Leonelli and Ankeny's (2015) concept of repertoire, and Fujimura's (1987) notion of doability. Both of which, I contend, can be drawn upon to investigate the process by which a robust epistemic culture emerges.

Like Knorr Cetina (1999), and indeed Kuhn (1962), and Clarke (1998), Leonelli and Ankeny's (2015) take on disciplinary, or research community, formation focuses on practice. They argue that common practices and infrastructure not only play an integral role in the formation of a discipline, but that a discipline's practical and conceptual norms provide, what they term, the blueprint for the way science should be done within that developing research community. Their concept of a repertoire can therefore, they argue, be thought of as, "a distinctive and shared ensemble of elements that make it practically possible for individuals to cooperate, including the norms for what counts as acceptable behaviors and practices together with the infrastructures, procedures, and resources that make it possible to implement such norms" and conduct research (Leonelli and Ankeny 2015: 701). By making it possible for individuals to cooperate on a set of common goals, the authors assert that it is just such a repertoire, with its material, social, and conceptual components, that first draws a research community together and then allows it to persist in the long term (Leonelli and Ankeny 2015). Given Knorr Cetina's (1999) assertion that, academic 'disciplines' and 'specialties' can be reconceptualised as epistemic cultures, I would argue that individual epistemic cultures can also be thought of as having repertoires.

The development of a repertoire is, Leonelli and Ankeny assert, "an important moment in the growth of a scientific community, in which key goals and values come to be explicitly articulated and efforts are aimed at making it feasible to achieve these goals" (2015: 707). Where Leonelli and Ankeny refer to this "important moment" as the development of a repertoire, Fujimura (1987) might argue that it is the moment when a problem becomes 'doable.' Introducing the concept of doability, Fujimura notes that "[s]cientists typically choose to pursue problems which are ripe, that is, both intellectually interesting and 'do-able'" (1987: 257). The doability of a scientific problem is established, Fujimura argues, through "the alignment of several levels of work organization" (1987: 258) with scientists needing to align factors at, what she terms, the experiment level, the laboratory level, and the wider social world level in order for a problem to be doable.

The concept of doability was discussed in chapter one but, in summary, Fujimura and Clarke (A. Clarke and Fujimura 1992; Fujimura 1987) contend that, in order for a scientific problem to be doable it not only has to be technically doable at the experimental level, but it has to be prioritised at the laboratory level, it must have the required infrastructure at the laboratory and social world level, and both the pursuit of the problem and the outcomes of the research must be viewed as worthwhile by those in academia, those in funding agencies, and those in the wider society where the research takes place.

Looking at this work on discipline formation more broadly it would seem that Leonelli and Ankeny's (2015) notion of a repertoire, as the set of social, conceptual, and material components which draw, and ultimately bind, a research community together, can be considered to be a necessary component within the broader strategy of making a research project doable. While both the building of a repertoire, and the rendering of a research strategy as doable, are key factors in the development of a resilient discipline with a clear and coherent epistemic culture.

Given the espoused hybridity of synthetic biology, the emerging discipline's repertoire, the problem it is attempting to render doable, and the epistemic culture it is forging, are all located at the intersection of biology and engineering. What is more, they are all predicated on the successful application of an engineering approach to biology. As discussed in chapter one, the introduction of this engineering approach within synthetic biology is most explicit in efforts to apply concepts such as standardisation, abstraction, and decoupling to biology, and the notion that novel biological organisms can be designed via modelling and then 'built' from standardised, hierarchical parts, devices, and systems. References to these engineering concepts, alongside the use of vocabulary and analogies drawn from engineering, are scattered throughout the synthetic biology literature, highlighting the pervasiveness of engineering ideas within the field (Arkin 2008; Baker et al. 2006; Endy 2005; Gibbs 2004; Serrano 2007). While the prevailing rhetoric suggests that all that is required for the successful emergence of the discipline, and its epistemic culture, is the simple enactment of this engineering ideal.

Indeed, in many ways synthetic biology already has the appearance of a distinct discipline with a robust repertoire, a doable problem, and a hybrid epistemic culture. After all it already has hybrid infrastructure, funding, and people. There are biological laboratories located in engineering schools, staffed by a mix of engineers and biologists. There are substantial grants and funding streams from, amongst others, the BBSRC[67] and the EPSRC.[68] There are journals and conferences, which draw authors, speakers, participants, and audiences from both sides of the discipline. There is a developing hybrid discourse, and hybrid research projects and strategies, which are garnering the backing of the UK government (Osborne 2012). Thus, from a distance, the lack of internal epistemic cultural cohesion within synthetic biology, identified in chapter three, is often obscured, and instead synthetic biology is presented as a sound discipline, built around the application of a straightforward, and rational engineering approach to biology.

This hallowed engineering approach, as it is described by the likes of Endy (2005), often underpins the prevailing rhetoric of synthetic biology. A dominant strand of the synthetic biology rhetoric which is found within the many articles ostensibly promoting synthetic biology as an emerging discipline (e.g. Andrianantoandro et al. 2006; Arkin 2008; Endy 2005, 2008), as well as reports and statements that address and describe the field (e.g. Bhattachary et al. 2010; Osborne 2012; UK Synthetic Biology Roadmap Coordination Group 2012). The rhetoric within such sources, focused as many of them are on discipline building, presents synthetic biology in an arguably

[67] The Biotechnology and Biological Research Council

[68] The Engineering and Physical Sciences Research Council

overly simplistic manner. Brushing under the carpet the very real difficulties of hybridising engineering and biology and of applying engineering ideas and methods to biology. Such difficulties are increasingly being acknowledged and discussed within the synthetic biology literature (see for example Bryner 2015; Silver et al. 2014; Way et al. 2014). However even these acknowledgements often go hand-in-hand with assertions that it is still early days for the discipline and thus it is only a matter of time before such difficulties are overcome. As such, despite the variation within the broader synthetic biology rhetoric, I would contend that, at this point in time, the notion that the 'engineering approach' can be, and will be, applied to biology remains prevalent.

Thus I found myself wondering how accurately this prevailing rhetoric represents the reality of the conceptual and practical norms, which are emerging within the discipline. Norms, which ultimately, support and shape the discipline, its repertoire, and its epistemic culture. Thus, just as I explored the day-to-day reality of the relationship between biology and engineering, so too did I explore the practical and conceptual norms emerging within the Centre, as those located within it attempted to apply their engineering approach to biology. What I found was a more complex, and interesting story.

Is biology 'engineerable'?

According to the prevailing rhetoric, a core component of synthetic biology's engineering approach is the adoption of standardisation, abstraction, and decoupling. As discussed in chapter one, these three core engineering concepts are being ushered into biology under the assumption that novel biological organisms can be built from standardised, hierarchical parts, devices, and systems. For example, it is believed by the likes of Endy (2005) that should biology be simply rendered into well characterised, standardised, interchangeable parts, then the building of new biological organisms will be significantly simpler and more predictable.

Once such standardised parts have been produced and characterised, it is maintained that their internal 'biology,' their nucleotide sequences, could be ‘black-boxed’ and ignored. Allowing those who work with them to treat them as discreet functional parts without the need, nor necessarily the knowledge, to tinker with them internally. The idea, drawn from software engineering, is then that these discreet, functional bioparts can be built into devices, and then into systems. Thus, ultimately producing synthetic biology products via a process referred to as the abstraction hierarchy (Endy 2005). As for decoupling, within engineering it refers to the separation of previously linked systems so that they can operate independently. Whereas within synthetic biology this translates to a desire to be able to separate the design and fabrication processes, so that those who design synthetic ‘constructs’ using computer modelling, are not necessarily the same people who render these designs as physical entities. Thus like abstraction, decoupling also relies on standardisation.

Yet, despite its ubiquity in early papers on synthetic biology (Andrianantoandro et al. 2006; Arkin 2008; Endy 2005; Heinemann and Panke 2006), there is a growing ambivalence to this model for the discipline. An ambivalence rooted in the belief that this model requires serious modification in order to be appropriate to biology. I encountered this ambivalence at workshops, such as the 2010 RoSBNet[69] meeting in Oxford, where during the breakaway groups people started advocating putting the rhetoric aside in order to actually discuss how problematic the approach really was. I also encountered it within the Centre. Michael, for example, raised concerns in relation to the use of the abstraction hierarchy within synthetic biology.

> *I’d say five, ten years ago it had a definite role as . . . a hypothesis for, ‘how do we make biology easier to engineer?’ . . . and the hypothesis was we do it the way we’ve done it in software, we do this abstraction hierarchy. . . . I think we’ve reached this point where it’s become this transition from a useful hypothesis to now it’s sort of neutral, I feel like soon it’s going to be on the harmful side when we start pouring*

[69] RoSBNet stands for Robust Synthetic Biology Network.

resources into this idea . . . it's just going to be an unproductive avenue.

(Michael, senior researcher, biology)

Michael's concerns stem from his belief that the abstraction hierarchy has outlived its usefulness in synthetic biology given that, to his mind, it does not make sense in terms of the underlying biology. Thus to continue to pursue it is, according to Michael, a waste of time and resources. As such, Michael and his research group have ceased using the term 'biological parts' completely.

In my group we don't talk about parts at all. I haven't talked about biological parts in five, six years, to be honest.

(Michael, senior researcher, biology)

Others at the Centre shared Michael's concerns regarding biological parts, as they are described by Endy. Martin, for example commented that, *"fundamentally BioBricks are a bit old-fashioned now."* However, unlike Michael most within the Centre had not abandoned this approach altogether. Rather, like Martin himself, they were seeking new, better, more feasible ways of assembling, characterising, and using bioparts. Thus, despite the general enthusiasm I encountered within the Centre for the application of an engineering approach to biology, every one of the synthetic biologists in the Centre acknowledged potential challenges in actually applying it in practice. Indeed many raised concerns that biology is either too complicated, or too unknown, for the successful and smooth incorporation of the engineering approach as it is outlined in the prevailing rhetoric.

Janet for example, a senior researcher with a background in biology, commented over lunch that she had noticed a general shift in the synthetic biology community away from the notion that biology can be engineered in the same way as inanimate products. Like Michael, whose rejection of the abstraction hierarchy was previously discussed, Janet questioned whether the parts, devices, and systems approach was feasible, and whether abstraction and decoupling were achievable. Yet she concluded that she was "*scared of saying that publicly*" as it may result in "*a chorus of voices saying the emperor* *has no clothes.*" Implying both that, the idea that biology can be engineered easily is like the fairy-tale of the emperor's new clothes, and that people believing this to be the case is something she wishes to avoid. For, while she concedes that the approach is problematic, being slow to apply and far from straightforward and easy, she still sees it as worthwhile. Others within the Centre, including Sam quoted below, echoed this mix of concern and commitment.

> *Biology is by far the most complicated thing . . . that engineering has ever been attempted to be applied to. So . . . we're still in the early days and the question still hasn't been entirely answered as to whether you can successfully apply engineering to biology. It may be that it's just too complicated and that we can't characterise things to the degree that we need to . . . The question is can you get around that with engineering or . . . can you incorporate it into your engineering approach in some way so that you can utilise that. Or at least not . . . intentionally go at loggerheads with it . . . I think we're still at the stage where people are confident that they can do this and apply engineering to biology but they're not quite sure yet . . . it might just be too complex to apply engineering to. But hopefully not!*
> (Sam, postdoctoral fellow, biology)

Difficulties in applying an engineering approach to biology are not, therefore, necessarily seen as deterrents, but rather, by the likes of Sam, as obstacles that need to be successfully negotiated in order to reach this ultimate goal. For Sam, a key to the successful engineering of biology will be working with the biology, rather than going "*at loggerheads with it.*" However for others at the Centre, as demonstrated in the quotes below, a key component in achieving this goal is the further alignment of synthetic biology with engineering, whilst subsequently distancing it from biology, and biologists.

> *It's basically just engineering but on biology, so . . . more than seeing synthetic biology as a field inside molecular biology, I prefer to see it*

as a new field inside engineering which draws from biology knowledge but really wants to just be engineering and not biology any more.

(Hayden, doctoral student, biology)

I think anyone with a healthy view of what synthetic biology is says that one of the main aims of synthetic biology is to get it out of the hands of the biologists.

(Martin, senior researcher, biology)

I think what [the Centre directors] *describe is less of a hybrid and more of an engineering* [discipline] . . . *and the biology is there sort of lurking . . . but you . . . try to ignore the fact that it's a biological thing that you're working with, and treat it as if it's not.*

(Janet, senior researcher, biology)

Hayden's, Martin's, and indeed the Centre Directors,' desires to align synthetic biology with engineering, and to put the control into the hands of the engineers, echo the aims and claims of Drew Endy. While Janet, it should be noted, did not agree with the approach she describes above. However, as more and more synthetic biologists are trained to view biology in this way Janet, and those who agree with her, may find themselves in the minority.

Yet, despite internal debates about whether synthetic biology can, or cannot, be engineered as readily as inanimate products, and whether it should be seen as an engineering or a life science discipline, every synthetic biologist I spoke to within the Centre acknowledged a prioritisation within the discipline of synthesis, over analysis. Such a research agenda would, according to historian of technology Walter Vincenti's description, align synthetic biology with engineering. "Engineering research," he writes, "has as its ultimate goal the production of knowledge useful for design (as well as production and operation); scientific research aims basically at explanation and understanding. As a result, research in engineering is pursued with different priorities and attitudes . . . It emphasizes application rather than illumination" (2006: 231). Such an emphasis on application rather than illumination was prevalent at the Centre, both in the way the synthetic biologists spoke about their work and the research projects they pursued. It is also clear in the following interview excerpts, as is the belief that this change in focus sets synthetic biology apart for more mainstream biology.

> *As I got interested and involved in synthetic biology I found that it did make me think about things in a different way . . . as a biologist you come at problems by wanting to understand biology . . . you want to understand the world, you want to understand how it works, and that's . . . just observational. . . . The synthetic biology aspect is much more . . . applied . . . it's not just looking at biology to understand it, it's then looking at it and thinking, what can I do with it? How can I use that as a tool? . . . I think it's part of why I enjoy it . . . I used to play with Meccano, I like building stuff, and synthetic biology is about building stuff.*
>
> (Peter, senior researcher, biology)

> *Biologists don't build things, they just don't build things! Biologists deconstruct things, they don't reconstruct . . . Engineers build stuff to do stuff, and this is this, but we're just using biological bits and bobs to build stuff and do stuff, so it has to be an engineering discipline.*
>
> (Malcolm, senior researcher, biology)

Here Peter and Malcolm not only outline ideas about what synthetic biology is, but do so by drawing attention to the ways in which they deem it to differ from biology. Something they are well qualified to speak on given that they are both senior researchers with backgrounds in biology. However, the acknowledged difficulties of applying an engineering approach in practice raised many questions for me, including whether the application of this approach is, in reality, primarily conceptual? Or whether there are, indeed, elements of the synthetic biologists' material practice that clearly set them apart from the biologists many seem determined to delineate themselves from? In order to explore these questions I began investigating the conceptual and practical manifestations of the engineering approach within the Centre, starting with discourse.

A new discourse for biology?

One of the first things that struck me about the synthetic biologists at the Centre was the way they spoke. After the very first lab meeting I attended, I wrote in my field notebook that, "*the language they use is fascinating.*" I was previously aware of the use of engineering terminology and analogies within synthetic biology from the synthetic biology literature (e.g. Andrianantoandro et al. 2006; P. Ball 2004; Endy 2005) and from public presentations (e.g. Man-Made Nature 2010; The Royal Academy of Engineering 2009). Ball, for example, uses terms like "retooling" proteins, "refitting" bacteria, "tuning" expression levels, and "tinkering" with the "building blocks" of genes and proteins (P. Ball 2004: 625). However, it was still striking to hear such ideas spoken aloud, so I started jotting down examples of this discourse whenever I could. Before long, amongst the many snippets of engineering-derived discourse I encountered, I had overheard the synthetic biology design and production strategy described in terms of an abstraction hierarchy of biological 'parts,' 'devices,' and 'systems;' I had heard cells being described as machines containing 'switches,' 'wires,' and 'circuits,' and I had heard them being compared to cars with mechanical and design features. This latter image was conjured by several members of the Centre, but perhaps most clearly by David during a journal club meeting when he described how he might go about designing an organism to have particular capabilities.

> *I want this powerhouse, this engine to go in my vehicle of the cell, and I then want this trim, or this steering system to go in it.*
> (David, doctoral student, biology)

As de Lorenzo and Danchin quite rightly note, "many synthetic biologists adopt the implicit or explicit metaphor of the cell as a complex mechanical machine" (2008: 825). The use of such discourse is, according to de Lorenzo and Danchin, part of synthetic biology's adoption of an engineering agenda, and is perhaps the most outwardly observable outcome of this adoption. In comparing synthetic biology's language to that of molecular biology, de Lorenzo and Danchin write, "[a]lthough molecular biologists often believe that their abstractions and representations - many of which are taken from physics - are the ultimate means to represent biological phenomena, their language might not be sufficient to fulfil the strong engineering agenda of synthetic biology." As such, "[a] robust language to describe engineering biological entities is needed" (de Lorenzo and Danchin 2008: 823). Aside from fulfilling their "*strong engineering agenda*," the use of this unique and common discourse can also be seen as a key element of synthetic biologists' repertoire and thus their discipline building efforts. For, adopting this novel language helps to set synthetic biology apart from similar biological fields, such as genetic engineering, that came before it but lacked, de Lorenzo and Danchin claim, "a common descriptive language" (2008: 823).

The adoption of a novel, common descriptive language, as part of discipline building, is however not new to biology. Keller writes that, in the 1950s, use of the information metaphor and its associated terminology served "as a means of demarcating the disciplinary boundary of the new molecular biology, especially from the traditions of biochemistry" (2000: 29). Thus in turn, synthetic biology's adoption of the engineering metaphor and its associated terminology can be seen as a means of demarcating the disciplinary boundary between synthetic biology and the traditions of molecular biology. However this is arguably not the only role that synthetic biology's new language plays in terms of disciplinary formation.

Aside from distinguishing synthetic biology from similar disciplines, the adoption of a new language also plays a role in creating internal coherence, providing a common language for those drawn to the discipline from engineering and from biology. The difficulties presented by not speaking the same language, which were discussed in chapter three, are encapsulated in the following quote from Max.

> *I think the other* [challenge] *is our ability to speak together. I think the way in which we communicate and understand each other is all-*

important for the field to survive, because unless we can feel like we get our ideas across – not as individuals, as a group – I think we're never going to succeed and we're going to . . . part ways again, because that kind of merging didn't work. But also I'd say that there are advantages to that whole breaking through the language barrier because . . . we can see what each other's doing and comment on it, and be separate but not completely distinct to each other's work and that, I think, is going to be the best way for the field to evolve.
(Max, doctoral student, biology)

According to Max therefore, and others in the Centre who echoed Max's claims, breaking through the language barrier so that all synthetic biologists regardless of background are speaking, or at least understanding, the same language is key for the coherence and success of the discipline. He argues that to try and merge the disciplines without merging the languages will not work, and will ultimately lead to the discipline splitting in two. He also however, sees shared language as an area of commonality that allows the two 'sides' of synthetic biology, while still separate from each other, to work together and avoid becoming completely distinct from each other. Thus I would argue that, for synthetic biology, the adoption of this common, engineering-inspired discourse is one of its developing repertoire's norms of behaviour (Leonelli and Ankeny 2015).

Yet, despite its roles in discipline building, in defining the scope of the discipline, and in reshaping the way synthetic biologists understand the natural world, such discourse does not necessarily come naturally to, nor does it sit well with, everyone within the field. I decided to sit in on the undergraduate synthetic biology course run by the Centre in order to get a better idea of how the discipline was being presented to students who may themselves enter the field in the future. During the very first class of the course Malcolm (senior researcher, biology) introduced the students to synthetic biology's engineering-derived discourse. Telling them that while "*biologists would never, ever use the engineering words that are used in the* *vision of synthetic biology,*" he hoped that the students would be "*familiar with them by the end of the course.*" He also warned them that, "y*ou will come to love it or hate it depending on your taste.*" Malcolm's comments stress several important points about synthetic biology's discourse. Firstly, that it is distinct from that of biology, secondly that learning it is deemed important, and thirdly that not all synthetic biologists like it.

While I did not encounter anyone within the Centre who spoke of either loving or hating synthetic biology's language, I did encounter some who were ambivalent towards it or feared it would prove detrimental to the field. This discomfort may have been due to a perceived disjuncture between the language itself and the underlying biological reality it was supposed to represent. De Lorenzo and Danchin highlight such a concern in relation to the synthetic biology concepts PoPS[70] and RiPS,[71] claiming, "they represent a straight and overtly simplistic projection of electrical engineering concepts into supposedly biological counterparts" (2008: 824). However, language use is not the only area where the overly simplistic projection of engineering concepts onto biology has proved problematic. As I shall discuss below, the ideas that such engineering language have heralded into biology, that biology is ultimately engineerable, are shaping both wet-lab and dry-lab[72] practices, but not without modification, compromise, and constraint.

Where's the engineering?

When I first entered the Centre's laboratories to undertake my fieldwork it had been seven years since I had finished my own studies in biochemistry, but the smell that greeted me immediately transported me back to my hours standing at a laboratory bench. The smell is hard to describe, slightly vinegary

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[70] PoPS stands for polymerase per second, a quantitative measure of the input/output signals of genetic circuits.

[71] RiPS stands for ribosomes per second, referring to the flow of translation machinery through messenger RNA.

[72] "Wet-lab" refers to the laboratory and is contrasted with "dry-lab" where computational and modelling work is undertaken.

and not entirely unpleasant, but instantly recognisable as belonging to a biological laboratory. Every weekday morning for seven months I would arrive on campus early, before most of the Centre's residents, and make my way up to the Centre's offices and laboratories on the six floor of the Engineering Building, and everyday I would encounter that smell. The senior researchers and lecturers would arrive first and then, as the morning advanced, the masters and doctoral students would file in, and the offices and laboratories would start to fill up.

Despite how busy they would become, the labs were generally quiet places, filled with white-coated individuals hovering around benches, working independently. Spectrophotometers would beep, freezers would hum, and centrifuges would whir. The occasional joke, or question would unite the inhabitants of one of the glass-walled laboratories in conversation. Such as the time when the PCR machine mysteriously started displaying the year as 1979, a cause of great hilarity as this time jump landed four years before PCR was invented. However, once the laughing, or problem solving, subsided everyone would return silently to his or her experiments. Running assay after assay, gel after gel, the synthetic biologists would toil away in the laboratories late into the evenings and over many weekends.

Milling around the Centre's laboratories, providing assistance with electrophoresis gels, PCR runs, and protein assays, I initially felt a tad confused. For, despite the synthetic biology discourse and rhetoric discussed above, at first glance the Centre's laboratories appeared to be just like any other life science laboratories, filled with the same sorts of people, doing the same sorts of tasks. Thus, given that synthetic biology defines itself by it's hybridisation of biology with engineering, where, I asked myself, was the engineering? For, with the exception of the Robot (which I shall discuss below), there was nothing that I could immediately identify within the wet-lab that would amount to my naïvely mechanistic notions of 'engineering.' Concerned that I was missing something I asked Andrew to point me towards the engineering and he patiently replied:

> *If you pin down someone working in the lab here and said, 'what engineering are you doing right now?' . . . they wouldn't know. But once you work in the field it does seem like the stuff you're doing that is engineering, like standardisation . . . that's all come from engineering, characterisation on that page* [pointing to the datasheet he was working on]*, engineering. But . . . you kind of take it for granted . . . like this is how it should be done . . . Engineering is a way of life . . . it's an approach, and* [synthetic biology] *is using an engineering approach.*
>
> (Andrew, doctoral student, biology)

It was the logical, taken for granted, though not immediately apparent nor easily identifiable, approach, which Andrew spoke of, that I needed to get to grips with. So, with Andrew's assessment ringing in my ears, I began to look more closely in order to explore this so-called engineering approach and how synthetic biology's drive to apply it was not only manifest in their language, but also within the physical laboratory environment.

Engineers in lab coats

Perhaps the most significant outcome of the drive to hybridise biology and engineering is, as shall be addressed in chapter six, the presence of engineers within the laboratories. However, despite the fact that these engineers have little or no background in biology, in their white lab coats and brightly coloured latex gloves, they are visually indistinguishable from the biologists. Yet, if you watch them closely as they work at the bench, there is a telltale hesitancy about them that marks them out from the biologists. This uncertainty is thoroughly understandable given that some of these individuals have never before set foot in a laboratory, nor experimented with living organisms, and thus they are learning very basic laboratory practices for the first time.

Since all synthetic biology projects within the Centre require aspects of both biology and engineering, all of the Centre's synthetic biologists, including those from engineering backgrounds, require at least a passing familiarity with biology, just as they all require at least basic knowledge of modelling. Some of those from engineering, especially those in senior positions, spend very little time in the laboratories, but others, such as the iGEM, Masters, and Doctoral students do, after their crash courses in biology and lab practices, begin to spend a significant proportion of their time at the bench. With time their hesitancy fades, and they begin to perform their experiments with ease and confidence, but this mix of biologists and engineers within the laboratories is nonetheless unusual. Indeed it is a feature that, in itself, sets the Centre apart from other life science laboratories I was used to. However a more headline-grabbing factor than the presence of engineers in biological laboratories is the presence of engineering driven projects.

Engineering biology in practice

As Andrew noted above, the engineering within synthetic biology is most readily observable in the use and development of standardised parts and their characterisation. Such parts were, as I will address below, designed, constructed, and characterised within the Centre, but what struck me most when I first entered the Centre, was that they would also arrive through the mail. On my first day as a Centre resident I accompanied Sara (doctoral student, biology) to fetch the Centre's parcels from the University mailroom on the other side of campus. The parcels themselves were not extraordinary, but the synthetic genetic constructs they contained struck me as such a clear sign of synthetic biology's engineering approach. These sections of DNA had been designed and ordered via computer and then assembled by a DNA synthesis company before being sent via the post to arrive within a matter of days of the order. I found it strange to think of these tiny stretches of designed DNA being pieced together, nucleotide by nucleotide, before winging their way through the postal service to be inserted into awaiting cellular 'chassis.' Yet, working alongside the synthetic biologists at the bench, watching them as they sought to characterise their 'parts,' listening as they discussed the benefits of various chassis, and assisting them as they ran repetition after repetition of their experiments, seeking results to plug into their mathematical models, I came to see that while such engineering was present in their work it was more complex that the prevailing rhetoric permits.

Indeed, in response to the growing ambivalence towards the 'Endy' model of engineering biology, more nuanced approaches to engineering biology have begun to crop up in the synthetic biology literature (Silver et al. 2014; Way et al. 2014) and in the research projects of those in the Centre. Where, rather than turn their backs on the notion of parts, devices, and systems, many at the Centre are tackling the problems they perceive with the abstraction hierarchy by modifying this approach in ways they deem more appropriate. Two doctoral students in particular, David and Christian, are clear examples of this strategy in practice.

During an otherwise ordinary day in the usually quiet laboratory David started getting very excited about his data, loudly exclaiming "*phwoar! That is heaven!*" as he examined an excel spreadsheet overlaid with small, colour-coded line graphs. David had been exploring growth rates of *E. coli* cell cultures at different volumes (200μL and 100μL) and his graphs, plotted from the plate reader data, were consistently showing the 100μL samples to be growing quickly before reaching a stationary state, while the 200μL samples were growing more slowly and not reaching a stationary state. I asked David why those with a lower volume grew faster and he explained that, due to their lower volume, there was room for a greater air supply and thus they were growing aerobically, whereas the higher volume cultures were growing anaerobically.

The importance of such work to synthetic biology, David explained, is that most of synthetic biology's standardised parts are being characterised while growing aerobically in flasks however, should they be scaled up for high throughput production processes they would likely be grown anaerobically in huge vats. Thus only knowing how they perform aerobically is, David argued, "*useless*." As you might have gathered, given his focus on characterisation, David's doctoral research falls well within the parts approach to synthetic biology. Specifically he is working on mapping out how different constitutive (rather than induced) promoters work under a range of conditions. As part of his experiments he is testing each of three different strains of *E. coli* in three different media and examining growth, both aerobic verses anaerobic growth, and the transfer from logarithmic to stationary growth. His interest in cell culture growth stems from his observations that modellers often feed into their models the assumption that the growth is consistent, something which David is busy proving does not match the biological reality. Later on the same day, still high on his results, David laid out for me his idea of a useful synthetic biology project. A project that would see the development of promoters that work between certain parameters of activity, rather than only at specific levels of activity. This, David contends, would allow for the fluctuation caused by different growth phases and thus would be a way of shifting synthetic biology's engineering work so that it is more in line with the biological reality.

Like David, Christian's doctoral research also falls within the parts approach to synthetic biology and, also like David, Christian is busy trying to correct some of the mistaken assumptions of synthetic biologists who hail from engineering. Christian is working on developing both a cell-free system, which can be used for bio-part characterisation, and a biosensor for detecting the presence of pathogenic biofilms that can spread infection. Christian's lab work involved mixing up stocks of his cell-free substrate, a chemical soup assembled using the contents of various bottles found on the shelf above him, and in the freezer below. The 'soup' itself includes all of the transcription and translation 'machinery' taken from lysed cells, but no actual living cells and no extraneous material such as cellular membranes. To this he adds the DNA of interest, the 'biopart,' and waits to measure the florescent output of the incorporated GFP[73] in order to determine whether or not the protein coded for by the DNA has been transcribed and translated.

Christian hopes to show that using his cell-free system is both easier and more efficient than using the in vivo systems, which are the current norm.[74]

[73] GFP stands for green fluorescent protein, a protein first isolated from jellyfish that glows green under light in the range of blue to ultraviolet. For more information see Tsien (1998).

[74] The in vivo system requires PCR, then the creation of a vector, insertion of the vector into a cell and then testing, whereas the cell-free system directly uses the PCR products for testing.

But more than just being faster and easier, Christian believes his system is more useful and appropriate for synthetic biology. The current system, Christian explained to me, produces vast amounts of information about each part being tested, however this information is frequently useless as it is based on the idea, drawn from engineering, that knowing how the part behaves in isolation is meaningful. Whereas Christian maintains that what you really need to know, when it comes to bioparts, is how they behave when they interact with, and alter, each other.

The cell-free system Christian is working on would instead provide a skeleton list of characterisation information about the part which, he believes, would be enough to be useful in modelling and would give you an idea of its function, but without spending too much time getting the detailed, and ultimately useless, information. Once parts had been combined into systems, Christian asserted, it would make more sense to characterise them more fully. Yet despite his conviction, Christian was concerned that he would not be able to make a strong enough argument for his case to convince those within the discipline who were committed to the current system. Christian's interest clearly lay in this foundational aspect of his project, however his supervisor, Malcolm, had insisted that he 'tack on' the biosensor work in order to have an application. This Christian put down to the Centre's "*obsession*" with the need for synthetic biology applications to come out of the research they performed.

These projects are but two of the many examples I encountered within the Centre where the engineering approach, specifically the parts approach to synthetic biology, was strongly evident. There were others within the Centre who, for example, undertook promoter characterisation under various conditions, addressed modular chromosome assembly methods, examined device-chassis interactions, and designed cell-free microfluidic systems for part characterisation. However I have focused on David and Christian's projects here as they highlight some of the myriad ways that synthetic biology projects are being shaped by the discipline's engineering approach. They also highlight the ways in which those at the Centre were trying to modify the engineering approach in order to make it more appropriate for the realities of biology, rather than the ideals of engineering. Yet, despite the complexity of applying an engineering approach to synthetic biology, which both David and Christian encountered and attempted to navigate, their projects also indicated the ways in which this same engineering approach is shaping the practical and procedural norms of those at the Centre. The questions they ask, the experiments they run, the equipment they use, the models they design, and the data they produce are all, as we shall see, underpinned by their embrace of the engineering approach.

Questions

Alan, one of the Centre directors, is adamant that "*synthetic biology is a technology not a science*" and that, in regards to bioparts, "*if you've got input-output characteristics, then that's enough, you don't need to know what goes on inside.*" Admittedly Alan hails from engineering himself, and is enamoured with the perceived potential of synthetic biology's engineering approach. However, as a guiding voice for the Centre his proclamation has power, shaping the questions those within the Centre ask, and the projects they undertake. As David (doctoral student, biology) explained, in regards to the engineering approach to biology that Alan heavily promotes, "*it's basically changed a 'what' question to a 'how' question*." David is referring here to a shift from the analytical questions predominant in biology, which address 'what' is happening in a system, to a greater focus on 'how' to make the system work. This shift towards addressing how to make systems work in order to use them for the purposes of production, rather than exploring the systems themselves for the purpose of knowledge generation, is evident in the drive to characterise bioparts that underlies both David and Christian's projects. It also underlies the pressure Christian felt to direct his project towards designing an application rather than the foundational techniques he is more interested in.

Experiments

The second way in which I observed the application of an engineering approach influencing the synthetic biologists' practice involved the experimental focus of their wet-lab work. The synthetic biologists were not just shaping their research questions around this approach, but also the way they went about exploring these questions. As detailed above, David was not only asking research questions about how best to characterise bioparts, he was also designing his characterisation experiments with an eye on which experiments would best provide meaningful data for future industrial production processes, rather than on which experiments would provide the most biologically interesting data.

For others within the Centre, the impact of the engineering approach on their wet-lab experiments saw them concentrating on aspects of interest to the modellers, but of no real interest for biologists. For Peter this meant experimentally exploring elements of a system that he would not investigate if he were still doing biology.

> *In terms of designing systems . . . it's not just about characterising this part it's about looking at what else is around that part and how that influences its behaviour . . . as a biologist you would not bother doing that experiment.*
>
> (Peter, senior researcher, biology)

The robot

A further, very visible sign of the Centre's adherence to the engineering approach, and to the goal of characterising bioparts, was the robot. A huge, heavy piece of equipment that sat upon its own reinforced bench along a wall of one of the laboratories. Alan (senior researcher, engineering) had bought the robot for 'his' lab, though I never once saw him in there. He was, perhaps, the member of the Centre least acquainted with the practices of a biological laboratory, but he knew machines, and the idea of automating and validating processes and results using a high throughput robot appealed to him. At least that is how David, who was one of his doctoral students, explained it to me. It was hoped that the robot would help with some of synthetic biology's more engineering driven quests, such as standardising and characterising biological parts. The problem was that not many people knew how to work the robot.[75] However this did not stop Alan buying another one, so that by the end of my fieldwork there were two robots, one for characterisation work, called C3PO, and one for assembly work called, unsurprisingly, R2D2. It was widely hoped that, with time and training, these two would become a central element of the Centre's experimental approach and data production. This hope was clear whenever groups from Industry, Engineering guilds, or other international Synthetic Biology centres would visit the Centre. For at these times, despite being seldom used, the robots became a highlighted, and much admired, tour stop.

Data

As with the research questions and experiments, taking an 'engineering' approach to biology, and embracing the kind of collaboration required by the field, also impacted on the data gathered in the wet-lab. At almost any time of the day you could find a member of the Centre hovering over a timer and carefully documenting, among other things, protein expression levels or optical density readings. Documenting such information is common in biology, but due to the desire for collaboration with the dry-lab work, several of the synthetic biologists at the Centre insisted that synthetic biology demands more systematic, rigorous measurements, more repeats of experiments, more standardisation, and more precision within the wet-lab work than biology. As Sara said:

> *If you want to take* [your experimental data] *into the dry lab and do the modelling . . . everything has to be super-accurate. You don't do that necessarily if you just want to express a protein in the lab . . . you don't do all the timing exactly.* [But] *you will have to do that if you're going to use the results in your model.*
>
> (Sara, doctoral student, engineering)

[75] At least, they didn't at the time that I started my fieldwork.

Thus from my observations of their day-to-day work it definitely seemed that, for the synthetic biologists working in the Centre, applying an engineering approach was not just rhetoric and discourse but rather was tangibly shaping their practices. Crafting the procedural norms of the discipline's repertoire, and thus strengthening its emergence. Indeed, even those who were uncertain of the applicability of the engineering approach, as Endy describes it, were working towards modifying the approach so that it would work. However I also came to see that, for the synthetic biologists at the Centre, 'taking an engineering approach to biology' equated to more than just altering their practices. Indeed, underpinning their shifts in practice was, I discovered, a shift in their way of thinking about the whole process of 'doing' and interacting with biology. A conceptual shift towards rationality that was likewise being shaped by the so-called engineering approach.

Rational design

The equation "Synthetic Biology = Engineering Biology" was written in marker pen at the top of the whiteboard in Grant's office. Contained, as it was, within a boxed outline it was clearly considered both important and not to be erased. Grant, an engineer by training with little previous knowledge of biology, was the Centre's resident modelling expert who embraced the notion of engineering biology as a practical strategy central to the synthetic biology endeavour. This perspective, I came to learn, was widely shared by his colleagues in the Centre, as well as others within the broader synthetic biology community. Indeed, during my fieldwork I encountered the 'engineering of biology' being described as both a "*revolution for biotechnology*" (Malcolm, senior researcher, biology), and as having "*moved past simple metaphor to become a reality*" (de Lorenzo 2010). Central to this perceived "*revolution*" and new "*reality*" were the tactics synthetic biology was drawing from engineering with the hope of "*controlling biology*" (George, postdoctoral researcher, engineering) and thus increasing the efficiency, efficacy, and rigour of synthetic biology's attempts to build complex biological systems. As Grant described it:

It's bringing this level of rigour . . . into biology. So it's trying to build systems of increasing complexity using a classical engineering approach, and actually seeing the fruit of it. Synthetic biologists really do get the point that if you take a rigorous approach for the building of this complex system you can indeed increase the complexity in a much more efficient way than it would be by just trial and error.

(Grant, senior researcher, engineering)

Taking such a rigorous engineering-inspired, research approach, it was hoped, would simplify 'construction' within synthetic biology, making it "*the biological equivalent of assembling Ikea furniture*" (Martin, senior researcher, biology), while also supporting the design and realisation of biologically novel functions within synthetic biology's 'products.' As Michael put it:

It's like, let's build new functions, let's make nature do what it doesn't do . . . what we haven't observed it to do yet . . . let's try to rewire or re-purpose the way that biology works, to do new things, interesting things, useful things.

(Michael, senior researcher, biology)

The idea of producing "*new*," "*interesting*," and "*useful*" things was, from what I could tell, behind much of the enthusiasm for synthetic biology's catch-phrase 'engineering approach.' And the driving concept within this approach was 'rationality.' Whenever conversation, during both interviews and informal discussions, turned to what it meant to engineer biology, 'rationality' and the taking of a 'rational approach' was almost always uttered. Lewis, for example, described synthetic biology's engineering approach as follows.

It's the ethos of engineering, . . . the idea that you build something up and the incorporation of modelling and sort of rational design . . . rational design is really key.

(Lewis, doctoral student, engineering)

For many, ‘rationality’ appeared to have become shorthand for describing the Centre’s ‘engineering approach’ to biology, an approach described as embracing rigor, reason, and logic.

The design cycle

Central to many of the Centre’s inhabitants’ views of how one incorporates a rational approach into synthetic biology is what they term, the design cycle, the engineering cycle, or the engineering design cycle. Christian, for example, described the rational approach like this:

> *So the cycle’s the best way to define it . . . you go from design into the modelling and into the construction and into characterisation of each of the individual parts, and then . . . iterations of that process. I guess that’s what’s new, right? Normally they do things in biology by brute force.*
>
> (Christian, doctoral student, biology)

Here Christian describes this engineering-derived iterative process to developing, testing, and evaluating ‘products,’ as what makes synthetic biology “*new,*” setting it apart from biology’s, apparently inferior, “*brute force*” approach. As depicted in figure 6, this design cycle, frequently rolled out in the Centre’s external presentations to describe their approach, begins with the identification of the specifications a ‘product’ must include. These specifications are then incorporated into a design for the ‘product,’ which is subsequently modelled before being ‘assembled.’ The physical ‘product’ is then, at least in theory, tested and the results are used to adjust the specifications for the next round of ‘tweaking’ which in turn alters the design, and so on and so forth until they are satisfied with the outcome. The premise is that adherence to this cycle of activities is the most efficient and rational way to design and produce an effective synthetic biology ‘product.’

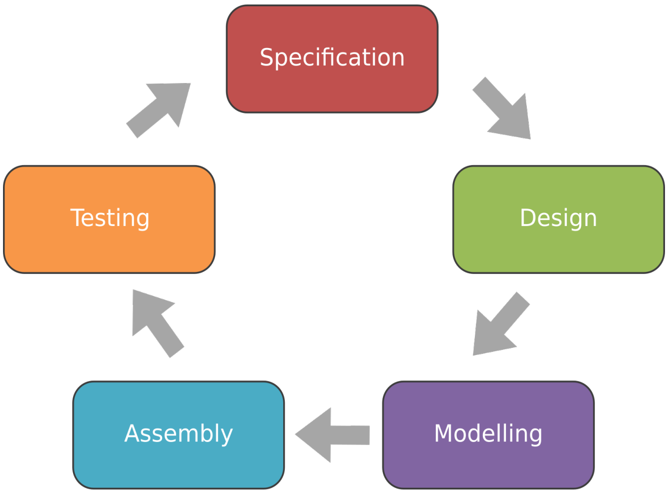

Figure 6: The engineering design cycle as theoretically applied to synthetic biology within the Centre

However from my observations of the day-to-day work within the Centre, it was apparent that the practice of synthetic biology was much messier than it was presented to be. For despite using the design cycle as a way of distinguishing themselves from other areas of biology, during my fieldwork I observed no examples of it being systematically applied. The challenging aspect for the synthetic biologists attempting to diligently follow the design cycle's steps was the modelling. As several of the synthetic biologists acknowledged, undertaking the modelling before the 'wet-lab' work, and actually using it to inform which experiments should be undertaken, was currently an ambitious goal rather than an accurate depiction of their process.

> *That's like the ultimate goal isn't it, to be able to have a system, but to model it first . . . but at the moment obviously you need data to model and it's that kind of a 'chicken egg' thing.*
>
> (Anna, doctoral student, biology)

> *You can't apply the engineering cycle. You can write that you apply it. And you can, but you skip the modelling bit basically. The specifications, 'this with this' kind of thing, that's all fine, but you are missing out . . . the modelling, which isn't in there, yet.*
>
> (Martin, senior researcher, biology)

Here Anna contends that the goal of modelling a system before you 'build' it is currently thwarted by the 'chicken or egg' dilemma that such models need to be based on the data produced by the systems they are intended to be designing. While Martin argues that this situation currently undermines their ability to apply, if not their ability to claim to have applied, the design cycle.

During my time in the Centre I observed two such occasions where, during public presentations, it was claimed that the design cycle had been faithfully applied in a project, but where in reality, the modelling was undertaken after the experimentation and was then slotted in as if it had preceded it. This is arguably an attempt to portray synthetic biology as more systematic, and 'rational' than it currently is, and thus to align it with the vision of engineering that these synthetic biologists are embracing. It is therefore tempting to proclaim that, given this gap between the practice of synthetic biology and its presentation as a rational, engineering discipline, the practice of synthetic biology and engineering have little in common. However several ethnographers have highlighted similar disparities between practice and presentation within engineering.

Bucciarelli (1994) for example contends that the vision of engineering as a rational, efficient, and systematic endeavour does not necessarily capture how engineering is really practiced, but rather how it presents itself. Bucciarelli argues that engineering is, in practice, much messier and more reliant on trial and error than engineers usually acknowledge, an argument that is supported by the works of Ravaille and Vinck (2003), and Blanco (2003), who show the design process in industrial engineering to be far from a linear, sequential process. Furthermore, Bucciarelli highlights the prevalence of, what he terms, "the incestuous character of this model-making process" (1994: 57) within engineering ("the model designed to verify field data; the data, in turn, providing a reference for the model" (1994: 57)), an observation that echoes Anna's 'chicken or egg' comment above. Thus it could be said that the gap between the reality and the projected image of the discipline aligns synthetic biology with, rather than distinguish it from, engineering. Indeed, as the following section highlights, although modelling is a central element of synthetic biology's engineering approach, like the design cycle, synthetic biology's relationship with modelling is far from straightforward and uncomplicated.

Modelling biology

The word 'modelling' comes from the Latin *modellus* and has long been used to describe a typically human way of coping with reality by reducing real world problems to simplified, artificial, representations (Schichl 2004). From at least the eighteenth century there have, however, been two main categories of models, physical models and mathematical models. Physical models were, at this time, used to represent the likes of humans and the heavens, while mathematical models were used for the likes of commerce and surveying (de Chadarevian and Hopwood 2004; Schichl 2004). Nevertheless, despite their differences, both types of models imitate some existing feature of art or nature, and both were predominantly used as teaching aids[76] (de Chadarevian and Hopwood 2004). With time, their use extended to include research, however until the twentieth century this was still in the capacity of description and characterisation (Schichl 2004). With the advent of computers there began a move from using physical models to using computer simulations to explore phenomena, and as the twentieth century progressed, and computer power increased, the distinction between physical and mathematical modelling continued to blur (de Chadarevian and Hopwood 2004). By the mid-twentieth century computer simulations had increasingly become the norm in the physical sciences and engineering, and the role of modelling had shifted from "one of problem *description* towards problem *solving*" (Schichl 2004: 31). However within developmental biology things were, and for that matter still are, markedly different.

Unlike the physical sciences, within developmental biology the term 'model' does not refer to a mechanical model, a chemical model, or to a set of

[76] For example, anatomy models were used to teach medical students, midwives, and artists, model machines were used to teach engineering, and model buildings were used to teach architecture (de Chadarevian and Hopwood 2004).

equations, but rather to an organism. Model organisms, such as mice, *Drosophila*, and *E. coli*, are not artificial constructs and, unlike within the physical sciences and engineering, the primary criterion for their selection as models is rarely simplicity. Furthermore, where models in the physical sciences and engineering are used to represent a class of phenomena, in biology, model organisms are used as models for a class of organisms (Keller 2002). Thus, Keller writes, biological modelling is sometimes described as "proceeding 'by homogeny' rather than 'by analogy'" (2002: 52). Yet within synthetic biology, this is beginning to change.

As historian of biology Michel Morange writes, one of the significant ways in which synthetic biology is novel in practice is that within synthetic biology, "models hold the position that they traditionally held in physics, ecology and evolutionary biology: they assist, support and guide the work of the experimenters" (2009: S52). It is the word 'guide' here that is particularly significant as synthetic biology is, as discussed above, striving to use modelling, as engineering does, for design rather than for representation. This is evident in the place modelling holds within the design cycle, and the centrality of modelling within the discipline's vision for its future. It is, as Lewis noted above, the combination of modelling and rational design that make up the Centre's engineering approach to biology.

Thus I spoke to Grant, the resident modelling expert, many times about the process and challenges of modelling within synthetic biology. As Grant explained it, synthetic biology needs models in order to "*efficiently design complex systems from the interconnection of well-characterised parts*," to "*easily predict the behaviour*" of these complex systems, and to "*propose ways to improve their behaviour*" (Grant, senior researcher, engineering). Yet there are "*no set rules*" for how to achieve this end. Grant, a control engineer, nevertheless has an approach, which he generally follows in order to provide what he calls "*rigorous results*" and "*performance guarantees*." Grant described this approach to me using the example of a modelling problem he had been working through with his students, and with the advice of Michael (senior researcher, biology). He had first met with Michael to discuss the problem to be modelled, and then he and his doctoral students and postdocs had defined the problem before returning to the biologists to check it made biological sense.

Grant told me that the process of modelling starts with an outline of what you want to do, this is the design phase in the design cycle. In this case, the project was seeking to maximise the flux of a metabolic pathway, so the first thing they did was draw up a mathematically simplified, and linear, model of the metabolic pathway. What they wanted to do was to branch the pathway off to create a new substrate, so they needed to figure out how much they could direct the flow of the pathway down the branch without killing the cell. Ultimately, what the modellers were trying to determine was how far you could push the system. Once they had defined the metabolic pathway in a model they looked at how they could optimise its output by running simulations with altered variables, this is the modelling phase. It was only after this point that they sought to render their mathematical models as physical entities by "*building*" the pathway in the lab in a step Grant referred to as the "*realisation process*," but which is referred to as the assembly phase in the design cycle.

At this point, Grant explained, they go through an iterative process to refine the model, moving back and forth between the lab and the modelling, the testing and specification phases. The modellers work out which variables they need to alter to gain the desired effects and then they go to the biologists to find overlap between what they, as modellers, want to adjust, and the variables the biologists actually can adjust in the system. Then they run experiments to test whether the adjustment in the model garnered the predicted output in the physical system. If it did not, there are several potential explanations. They could have missed out a single variable, or multiple variables, from their model, or the biologist doing the wet lab work could have made a mistake. Once they figure it out they adjust the model as necessary and do it again until it behaves as predicted.

As Grant explained it, if you do it right 80-90% of the effort of modelling is in defining the problem, and the other 10-20% is finding the solution. This should then render a "*good*" model, one that is accurate, predictive (meaning the outcome of the model, obtained through analysis or simulation, is very close to the real system outcome), reusable in other similar cases, and parsimonious (meaning it should be as simple as possible). "*This*," Grant claimed, "*allows us to develop synthetic biology in the same way as other engineering disciplines*." Yet, despite his confidence Grant admitted that there are challenges to the successful incorporation of modelling into synthetic biology. The challenges Grant highlighted originate from the changeable nature of the material being modelled. How, for example, do you mathematically capture evolution, or model self-replication and stochasticity? These are indeed significant challenges for modelling biology, however there are other challenges that Grant did not mention. Challenges that stem from the trade off between accuracy and simplicity, and the need for standardised and characterised parts.

On the first page of his lecture notes for a course on modelling biology, Grant has printed the following George Box[77] quote, "All models are wrong, but some of them are useful." Grant explained to me that, the key to designing useful models was "*to be able to judge the right degree of abstraction to apply so that you simplify the model as much as possible, but no more than is necessary. You must*," he continued, "*capture the most important phenomena, but only the most important phenomena as you can't model every single element of a biological system*." This need to simplify a system in order to model it was, at times, a cause of frustration within synthetic biology, especially when those in the wet lab were told that the data they had meticulously collected was not required. As Martin put it, "*it is depressing to gather huge amounts of data to give to a modeller who then says 'this doesn't matter, and this doesn't matter', as they are only looking for bottlenecks and important parameters in order to simplify the system*." Yet, while this is potentially a challenge to the development of cohesive, collaborative relationships within synthetic biology,

[77] George Box was a famous British statistician.

a greater challenge for the role of modelling in the discipline is arguably its reliance on well-characterised parts.

One afternoon Simon and Christian (both doctoral students hailing from biology) were sitting at their computers talking over their own experiences with modelling. They stressed that what you want, in synthetic biology, is predictive models, those that determine and predict the experimental processes and outcomes. This, after all, is what the design cycle calls for, and what Alan (one of the Centre directors) advocates. However in reality, as addressed above, such models are hard to develop. Simon and Christian explained to me that the difficulty was in large part due to the dearth of available standardised characterisation data. Collaborations such as BIOFAB,[78] and members of the Centre such as David, were working towards this, but there was still a lot of work required before all of the desired parts were characterised using the same units, and providing the same detail under the same conditions.

The dream, they explained, was to have sufficient underlying characterisation to allow drag and drop CAD[79] modelling tools, such as Tinkercell,[80] to be workable. But, in reality there was not yet enough data to realise this dream.[81] Christian and Simon thus confessed that, while modelling for design and control was undeniably the aim of synthetic biology, and is frequently claimed to be the reality by those within the Centre and the wider discipline, models have yet to achieve this centrality and status in reality. Nevertheless better, and more plentiful, characterisation would, they asserted, make modelling more accurate and would increase the likelihood that modelling could usefully and feasibly be done before, rather than after, the

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[78] The BIOFAB: International Open Facility Advancing Biotechnology is a collaborative endeavour to produce standardised, biological parts for academic and commercial users (SynBERC).

[79] Computer Aided Design.

[80] Interestingly, TinkerCell is no longer being actively developed. However it is uncertain whether this is because of the challenges mentioned above (Chandran).

[81] In the meantime those within the Centre predominantly used a modelling program called SimBiology, which relies on the programming language MatLAB.

experimental work. Thus allowing modelling to slot into its 'proper' place within the design cycle, a place from which it could precede and guide the experimentation rather than follow and support it. As such, it was this desire that was guiding and shaping the conceptual and practical norms of those, like David, who were working to develop such standardisation and characterisation of bioparts within the Centre.

Thus like the abstraction hierarchy, and the design cycle, modelling is another key element of synthetic biology's engineering approach that is a lot more complicated in reality than the prevailing rhetoric suggests. However, and as discussed in chapter three, it is not only these engineering elements that are proving a challenge for the realisation of the discipline and its hybrid epistemic culture. Rather, due to the epistemic cultural differences of those who have entered the field, those within the Centre were also struggling to overcome the challenges of collaboration.

Collaborative compromise and constraint

As highlighted in chapter three, collaboration is, currently, a basic requirement in fulfilling the demands of taking an engineering approach to biology, and thus establishing synthetic biology as a discipline. Indeed, at this point in the discipline's emergence, a point where the necessary skill set and knowledge base for the discipline is not ubiquitous, but rather is largely spread across two separate internal groups, collaboration is key. Thus, just as shaping their work around the abstraction hierarchy, the design cycle, and the ambitions of the modellers is, ultimately, establishing practical and conceptual norms for the synthetic biologists, so too are their norms being shaped by their collaborative working relationships. For it is frequently within these relationships that those at the Centre strive to enact the engineering approach in practice, dividing the wet-lab and dry-lab aspects of the work amongst themselves. Yet, while these relationships help to determine the norms and shape of practice for the synthetic biologists at the Centre, allowing them to implement the engineering approach, I came to learn that the consequent demands and frustrations of the collaboration, constrained their work and potentially restricted the promise of synthetic biology.

One day while talking to Lewis about his experiences of collaboration, he told me, as Anna had before, that in each project the two 'sides' have to compromise and adapt to fit each other. Yet, Lewis stressed, while the hope of synthetic biology is that this will lead to added value, the very real risk is you end up with "*a second rate model, and a second rate lab study*" (Lewis, doctoral student, engineering). With Lewis' words in the back of my head, I began asking others about their own experiences. In responding to my question of whether there were any downsides to collaborating with biologists in order to implement the engineering approach to biology, Stephanie (senior researcher, engineering) responded without hesitation that, "*just working with biology constrains our work.*" This, she explained, was due to a lack of understanding of how biology 'works' and a dearth of attainable data.

Where Stephanie voiced the opinion that attempting to take an engineering approach to biology constrains the work of engineers, Peter made the opposing assertion that working towards this goal also constrains the biological work.

> *Some people work on systems that are simplified biologically . . . so that it's a tractable modelling problem, which is good, I mean in order to learn you have to start with the simplest system and then build up to the complex system that you want to be working on. . . . Probably that's the reason why synthetic biology has focused a lot on the mono-systems that it has . . . and they've stayed away from systems that are maybe more industrially relevant . . . because . . . nobody knows what's going on inside those, and so then you'd have to start at square one and find all that information out before you could use it.*
>
> (Peter, senior researcher, biology)

Here Peter is highlighting the challenge that, due to the hybrid nature of the emerging discipline, a successful synthetic biology project must be both feasible in the laboratory and a "*tractable modelling problem.*" Thus, given that a biological system must be understood, in order to be modelled, synthetic biology has, so far, largely been limited to simple, well-understood biological systems rather than the more industrially relevant ones. This was a point that Michael also struck upon when he said:

> *I mean honestly I think that* [taking an engineering approach] *probably restricted* [the field]*, it's probably slowed it down, so you've got a large part of the field looking at E. coli . . . because it's well understood and we know how to work with it.*
> *(*Michael, senior researcher, biology)

As highlighted by these quotations, I came to learn that the limited understanding and data available from biological experiments was believed by some to have restricted the work of engineers attempting to produce models for synthetic biology. Whereas the discipline's emphasis on standardisation and the use of simple, well characterised, biological 'chassis,' has benefited both the modelling and the work to improve the reliability, predictability, and reusability of the entities they 'construct.' However, it has theoretically, also simultaneously constrained the field's potential to produce the industrially relevant systems it strives for.

Deskilling

Another potential way in which synthetic biology's drive to implement an engineering approach to biology may prove to be constraining is the deskilling of those from biology. A professional, rather than a practical or epistemic consequence of such a merger, this concern was raised, several times, during my fieldwork both by those within the Centre and those within the greater synthetic biology community. At an Open Source Biology workshop in 2010, for example, historian and philosopher of science Bernadette Bensaude-Vincent commented, during her presentation, that, "*Endy's focus on simplifying biology for engineering results in a deskilling.*" Sociologist Nikolas Rose echoed this observation at the same meeting, when he noted that the deskilling of craftspeople was central to the Industrial Revolution. Thus, if, as

Alan contends, synthetic biology is to be the next industrial revolution it will involve the deskilling of biology and, therefore, its downgrading of authority.

It would be tempting to assume that these were solely the concerns of social scientists were it not for the fact that they were also expressed by several members of the Centre. Christian (doctoral student, biology) for example, expressed his unease that the discipline he was aligning himself with, was striving to do away with the need for his skills. While Janet (senior researcher, biology) similarly stressed that if synthetic biology succeeds in its goals of abstraction and decoupling, so that people only need to understand the small piece of the process they work on, "*the resultant deskilling of biology could be severe*." Apparently Syngenta[82] attempted to turn its lab work into just such a production line a few years ago. However Karen wasn't certain whether they had managed to recruit people to do, what she termed, the "*mind-numbingly repetitive tasks*." If synthetic biology went the same way, Karen stressed, she feared no one would want to do it anymore.

Building a collaborative discipline

The acknowledged limitations and challenges of the engineering approach, the constraints of collaboration, and the risks of deskilling half of the discipline's adherents, all arguably pose risks to the successful emergence of synthetic biology as a viable discipline. On paper, these factors appear to undermine both the attempts to draw the two sides of synthetic biology together in order to form a coherent repertoire, and the efforts to establish synthetic biology's defining problem, the application of an engineering approach to biology, as doable. Yet, I observed that the determination to do just this remained. Indeed, in spite of these challenges, the pervasive desire to develop and use standard chassis, standard methods and develop standard parts in synthetic biology was seen by some within the Centre as a way of drawing the disciplinary community together, a topic explored by Calvert

[82] Syngenta is an international biotechnical agriculture company.

(2010a). Hayden, for example, addressed this relationship between standardisation and disciplinary community building, when he said:

> *It's like the way you design experiments and the way you set your goals. For example when I'm trying to develop an assembly system for genes, instead of just . . . developing something that only works for us,* [I think] *'could this system work for anybody else, could this be used by anybody else, could this become a standard in the field?' And this guides the way I think. . . . If you're just in a lab doing research for yourself you don't really think of that, you just get your data, get your paper out – you still do good research but it's not . . . aimed at building something that can be used by other labs to all work in concert towards one goal, one application.*
>
> (Hayden, doctoral student, biology)

Further signs of the commitment I encountered to making synthetic biology 'work' as a discipline can be seen, as detailed above and in the previous chapter, in the way members of the Centre increased their workload, adapted their research questions, experiments, data collection methods, and models for the benefit of their colleagues and their collaborative projects. Here Hayden is simply referring to this same work being done on a disciplinary level. He highlights a desire to standardise synthetic biologists' work so that together, as a discipline, they can achieve their common goal of producing industrialisable applications. A goal that would not only support the development of synthetic biology's repertoire, but would also see synthetic biology further aligned with engineering and distanced from biology.

Idealised engineering

The drive to align synthetic biology with engineering rather than biology was almost palpable within the Centre, and came through loud and clear in my fieldwork and interviews. Above we heard that unlike biologists, whose work is described as "*just observational*" given that they "*never build new things,*" synthetic biologists' work is considered "*applied,*" "*using biological bits and bobs to build stuff and do stuff.*" Previously we saw synthetic biology described as "*rigorous*," "*industrially useful*," "*efficient*," and "*rational*," while biology was said to use "*trial and error*" and "*brute force*." The adjectives applied here to synthetic biology are drawn from an idealised notion of engineering appropriated by many of the synthetic biologists at the Centre and used as a counter position to a derogative notion of biology. Grant (senior researcher, engineering) painted this comparison most starkly when he described the biologist's approach to problems as being "*haphazard and almost violent,*" while that of the engineer as "*systematic and logical.*" Many biologists, and I dare say some within the Centre with a background in biology, would challenge Grant's description of biology, but less would perhaps challenge his description of engineering. Yet, as we saw above, this notion of engineering is also out of step with the messy reality of engineering.

Furthermore, as we also saw above, synthetic biology is, at least at present, not as rational, rigorous or efficient as it is frequently described to be. Thus, like the use of the novel, engineering-derived, descriptive language discussed above, these proposed disciplinary distinctions, and the inherent alignment with engineering, are arguably more of an endeavour to demarcate the emerging discipline of synthetic biology as something new and distinct from biology, than an accurate description of their differences. As Mackenzie suggests, such a desire to embrace 'rational design' and the engineering-inspired techniques considered to enable such an approach to their work, may highlight the synthetic biologists' "underlying apprehension of the inefficiency or 'irrationality' of trial-and-error approaches to creating biotechnologies and drugs" (2010: 192). Thus adopting this engineering approach and invoking rational design principles, "demarcates synthetic biology from genomic science and biotechnology more generally by borrowing a form of legitimation derived from the manifest success of engineering design in many domains. It promises products rather than experiments" (Mackenzie 2010: 194).

Therefore, despite concerns that biology is resisting being engineered, and thus acknowledgements that applying an engineering approach to biology is challenging, the synthetic biologists at the Centre largely embrace the belief that the engineering of biology will ultimately prove to be doable. For many of them, appropriating engineering's supposedly efficient, rigorous and logical approach presented a revolutionary way of interacting with, and controlling, biology. Thus in striving to achieve this ends, the synthetic biologists at the Centre variously employed strategies such as prioritising synthesis over analysis; embracing notions of rationality and standardisation; attempting to faithfully adhere to an engineering-derived design cycle; and endeavouring to align themselves, and their venture, with engineers and engineering and distance themselves from biologists and biology. Yet the key words here are 'attempting' and 'endeavouring,' for despite their commitment and efforts those at the Centre were unable to fully apply their idealised version of engineering to biology.

A kludged engineering approach

Indeed despite the prevailing rhetoric, which maintains that synthetic biology employs a robust, efficient, rational engineering approach, the reality I encountered within the Centre was a lot messier, and arguably a lot closer to kludging. Kludging, a concept drawn from engineering, purportedly originated as an acronym for "a workaround solution that is *k*lumsy, *l*ame, *u*gly, *d*umb, but *g*ood *e*nough" (O'Malley 2009: 382). Thus given the reality of synthetic biology, with its iterative rounds of trial, error, and pragmatic solutions, O'Malley argues that the engineering approach that is currently employed within the emerging discipline ultimately aligns more closely with kludging than it does with rational, elegant, efficient design.

This tension between the rhetoric and reality of synthetic biology's engineering approach brought to mind Rheinberger's (1997) assertion that scientists are bricoleurs, or tinkerers, rather than engineers. That is, they do not create the efficient, rational designs and solutions preferred by engineers. However, this assertion assumes that engineers do produce such idealised designs and solutions. An assumption called into question by Bucciarelli's (1994) work, discussed above, which suggests that engineers actually do a lot of what could be called kludging themselves, even though they seldom admit to it or openly frame their work in this way. O'Malley addresses this unspoken commonality between biologists and engineers asserting that "[e]xperimental kludging and model 'fudging' do not make biologists inferior to engineers, however, because . . . many sorts of engineers kludge to make things work" (O'Malley 2009: 383).

Furthermore, O'Malley is adamant that to say synthetic biology's engineering approach amounts to kludging, rather than to rational design, is not to say that such kludging equates to failure. Rather such kludging is "a highly creative and effective process" (O'Malley 2009: 382), and one that not only makes things work but does so "often in the context of non-standardized parts and insufficient knowledge" (2009: 383). Thus the key aspect of the 'kludge' acronym may indeed be 'good enough.' In that, their solutions may not be elegant but they seem to be working. However, O'Malley also notes that despite the creativity, and efficacy, of the kludging process, "synthetic biology is in many respects antikludge: it wants nature and engineering to be elegant and efficient" (O'Malley 2009: 383). As such synthetic biology clings to its idealised notion of engineering, even though this fits with neither engineering itself, nor with synthetic biology's application of engineering.

Similarly, despite the 'antikludging' rhetoric they espoused, which suggested that synthetic biology is defined by its application of a rational, efficient, and elegant engineering approach to biology, the reality I discovered within the Centre was a lot messier. No single element of the engineering approach was applied without modification in order to find some way of making it work. Not the abstraction hierarchy, nor the design cycle, nor the modelling. Nothing was straightforward, nothing was elegant, and nothing was 'rational' as such. Though, as demonstrated in the 'cleaned up' presentations of the design cycle, which hid from view the kludging which had taken place in its application, those at the Centre were not keen to openly jettison their idealised version of engineering in favour of a kludged version. Nevertheless, the kludged version of an engineering approach they were applying in reality was still seemingly shaping the work and outputs of the Centre. Indeed, although the engineering approach wasn't as easy to achieve as the prevailing rhetoric maintains, those at the Centre were, giving primacy to the role of modelling, forming new collaborations, asking new questions, using different experimental designs, and collecting new levels and types of data. All of these conceptual and practical norms were underpinned by their kludged version of engineering, and all were furnishing the emerging discipline’s repertoire, increasing the doability of their problem (the application of an engineering approach to biology) and thus helping to establish its epistemic culture.

While this hybrid epistemic culture is yet to fully emerge, I would argue that the key elements for its formation are assembling. There is the academic identity of being a synthetic biologist, and undergraduate courses and graduate degrees to furnish the discipline’s ranks. There is the hybrid discourse, drawing terms from engineering and applying them to biology. There are the practical and conceptual norms, underpinned by a kludged version of engineering, which are shaping the projects, outputs, collaborations, and general day-to-day work of synthetic biologists. And there are research units, like the Centre, which are equipped with the funding, infrastructure, and profile to promote the existence and coherence of the emerging discipline. However, while this momentum appears to be leading towards the full emergence of synthetic biology as a notable discipline, with a robust repertoire, a doable problem, and a distinctive epistemic culture, this is not to say that biology will prove to be engineerable in the way the prevailing rhetoric maintains. That is, for all their application of engineering, it remains to be seen whether synthetic biology can successfully design and build reliable, predictable organisms using solely standardised, well-characterised parts. Furthermore, as addressed above, while their attempt to apply standardisation and rationality, albeit in a kludged form, may aid community building and the transformation of synthetic biology into a coherent discipline aligned with engineering, it may also have the unintended outcome of restricting the discipline’s scope.

Conclusion

Within the academic synthetic biology research centre where I conducted my study, the adoption of an engineering approach to their work was strongly promoted by the directors and embraced by most. Taking an engineering approach to biology, for many within the Centre, meant attempting to adopt an efficient, rigorous and logical approach to their work appropriated from an idealised version of engineering. The adoption of this approach was perhaps most clearly manifest in the engineering-derived language the synthetic biologists used to describe their own, and the discipline's endeavours.

This common language, which draws heavily on metaphors and terminology from engineering, contributes to the formation of the synthetic biology's repertoire and thus its emergence, by aiding cohesiveness within the discipline, while also delineating synthetic biology from other disciplines. Furthermore, it arguably helps to shape synthetic biology's scope and the synthetic biologists' understandings of the natural world. However, as discussed above, adhering to the engineering approach to biology, and to its accompanying language, is easier said than done. Biology, the members of the Centre agreed, is much more difficult to engineer than inanimate materials, and applying engineering-derived terminology, concepts, and modes of work, to biology is a significant challenge.

This gap between rhetoric and practice, which is arguably a significant obstacle to the application of the idealised engineering approach, was perhaps clearest in the enactment of the design cycle. This engineering-inspired cycle of production dictated that dry-lab modelling work should proceed and guide wet-lab 'assembly' work. However, given the 'chicken or egg' relationship between biological data and modelling within synthetic biology, whereby the models are currently based on the data produced by the systems they are intended to be designing, the cycle is not, currently, being faithfully applied. Applying the design cycle in practice was therefore a significant challenge to the synthetic biologists' aim of applying an idealised engineering approach to biology. However, the synthetic biologists at the Centre remained determined to find ways around such challenges.

Thus, despite the obstacles they faced in regards to the application of the abstraction hierarchy, the design cycle, and modelling for design and control, the synthetic biologists continued to embrace the notion of applying an engineering approach to their work. Moulding their day-to-day practices around the aims of the discipline, they let their engineering approach shape the questions they asked, the experiments they conducted, the models they produced, and the data they collected. They also let it shape their working relationships, such that collaboration has come to play a central role within the discipline. However, given the modifications and approximations they have needed to apply to their idealised engineering approach in order to 'make it work' as best they can, I argue that the engineering approach which is shaping their work, and thus the discipline of synthetic biology and it's emerging epistemic culture, is a kludged version of an engineering approach. An engineering approach which is klumsy, rather than elegant, which is defined by trial and error rather than rational design, but one that, while it may not be efficient, is still proving efficacious in shaping the discipline and its products.

Yet despite the current success of their kludged engineering approach, O'Malley (2009) asserts that synthetic biology remains staunchly anti-kludge. I indeed found that many at the Centre believe, or at least hope, that biology will ultimately prove to be engineerable in the idealised fashion. To this ends, they prioritise synthesis over analysis, and adopt terminology and concepts drawn from engineering as they strive to use an efficient, rigorous, and logical approach to controlling biology and producing, novel, industrialisable 'products.' The desire to produce such 'products' goes some way to explaining attempts to cast synthetic biology as an engineering discipline, thus aligning it with engineering while simultaneously distancing it from biology. Indeed the Centre's drive to align themselves, and synthetic biology, with engineering was so strong and universal that it trumped the power dynamics at play between the two 'sides' of the Centre.[83] So much so that I would contend that their

[83] As evident in the beliefs of some individuals' that the contributions of their 'side' of synthetic biology were more important than those of the other 'side,' and in the disparaging stereotypes employed by each 'side' in regards to the other (both of which were discussed in chapter three).

primary motivation in striving to turn synthetic biology into an engineering discipline was one of discipline building. An attempt, as I see it, to distinguish synthetic biology from biology, and molecular biology in particular, which draws on the legitimation derived from engineering's success as synthetic biology strives for its own. Even though such a goal brought with it the risk of deskilling the biologists.

Thus, it could be said that such determined attempts to apply an idealised version of engineering to biology, to hide from view the instances of kludging, to stifle their doubts for fear of others concluding that 'the emperor has no clothes,' and to aligning synthetic biology with engineering, are helping to establish the discipline of synthetic biology. This is achieved by delineating synthetic biology from other disciplines while also building its repertoire through the establishment of practical and conceptual norms. Albeit norms which are based on kludging. Thus I would ultimately contend that synthetic biology is an emerging interdiscipline whose developing epistemic culture is founded on hybrid language, research centres, personnel, and funding, and conceptual and practical norms which are underpinned by a kludged, rather than a rational, engineering approach to biology.

Chapter Five: "*Machiney-something-elseys*:" Examining the 'products' of synthetic biology

Each and every one of the Centre's laboratories is teeming with life. Not just the senior investigators, post-graduate researchers, and doctoral and masters students who, white coated and concentrating, move from bench to bench, but also the countless colonies of microorganisms that occupy petri dishes and test-tubes in the Centre's many fridges, freezers, and incubators. These organisms, fed and nurtured to assist their reproduction and survival, are being designed and bred to perform certain, pre-defined tasks. It is hoped that some will glow green when encountering pathogenic biofilms, while others are having their constituent genetic material whittled away with the aim of producing minimal cells, a new kind of cellular 'chassis' if you will. There are organisms that are being designed to overproduce carbohydrate material polymers, and organisms that are being devised to act as *in vivo* biosensors to monitor and control cellular behaviour. All of these organisms are alive and, despite all attempts to control them, they are undoubtedly, like all biological organisms, mutating and evolving. Yet, all of these organisms are also being designed and modelled using engineering practices with the hope that they will perform predictably and controllably, much like machines. It is here then that the epistemic clashes and conceptual differences between synthetic biology's two sides, biology and engineering, become embedded within the discipline's 'products,' the organisms themselves. And it is here too that the tensions between synthetic biology's reductionistic approach to biology, and the conceptual and practical challenges caused by the deficit in our understanding of life come to a head.

As discussed in chapter four, synthetic biology explicitly aims to take an engineering approach to biology, and thus make biology engineerable, but where does this leave the resultant 'engineered' organisms? Do the synthetic biologists at the Centre see the 'products' of their work as machines? This would arguably be the logical end point of believing you can engineer biology like any other inanimate material after all. Do they instead see them as organisms, admittedly nudged in certain biological directions, but essentially no different from naturally occurring 'wild' microorganisms? Or indeed, do they see them as some kind of hybrids that ultimately blur the age-old machine/organism divide? As shall be discussed in detail in chapter six, synthetic biology appears to be part of a more general epistemic shift towards a view of life as engineerable material, a shift that is accompanied by a commitment to applying engineering discourse and methods to biology. The notion of life as engineerable material, central to this potential epistemic shift, implies that the 'material,' in this case biological 'parts' and biological organisms, is essentially no different to other engineerable materials. Such a shift towards an engineering epistemology, therefore, suggests a step, and potentially a large step, towards blurring or even removing the conceptual boundary between machines and organisms. What, I therefore wondered, does such a shift mean for the synthetic biologists at the Centre's conception of 'life?' How, that is, do they think about, and categorise, the living 'products' they are designing, producing, and sharing their lab space with, and how do their views fit within the messy, uncertain, contentious history of the machine/organism divide?

On May 20th 2010 all of these questions, which had spent months running around my head, came crashing to the fore. It was only my second day of intensive fieldwork, and I was still figuring out the lay of the land as the newest inhabitant of the Centre. Unusually the normally quiet laboratories and offices were abuzz. There were film crews interviewing Alan and Malcolm (the Centre directors), and journalists seeking comment from the Centre's senior members. Craig Venter, of the J. Craig Venter Institute, had just announced that his team had successfully 'booted up' a synthesised version of the *Mycoplasma mycoides* genome within another cell (reported in Gibson et al. 2010). At a press conference that day Craig Venter described the resulting organism as "the first self-replicating species we've had on the planet whose parent is a computer" (quoted in Wade 2010) and this notion of a machine/organism hybrid was doing the rounds. Eager to find out how the story was being depicted in the media, David (doctoral student, biology) and I set off across campus the next morning to buy a copy of every newspaper we could find with a reference to the announcement. There were claims that Venter and his team had variously made artificial life (e.g. Sample 2010), synthetic life (e.g. Connor 2010; Henderson 2010) or man-made life (e.g. Alleyne 2010), and many questions about whether Venter was 'playing god' (e.g. Alleyne 2010; Connor 2010; Morton 2010) or indeed playing "Frankenstein" (Dawar 2010; Morton 2010). The front page headline of The Guardian referred to Venter as "God 2.0" (Sample 2010) while that of the Metro called him "Dr God" (Attewill 2010). The front cover of The Economist, issued two days after the announcement, even depicted David, with a laptop on his knee, creating cells under the headline, "And man made life" (2010) (see figure 7).

Figure 7: Front cover of *The Economist* May 22nd-28th 2010

The 'synthetic' organism Venter and his team 'created,' which quickly gained the name 'Synthia,'[84] prompted a worldwide debate and discussion over what exactly the 'products' of synthetic biology are, how we can classify them, and how we should feel about their creation. As the headlines quoted above suggest, this breakthrough from the J. Craig Venter Institute raised as many conceptual questions as scientific questions.

In literature, and in history, creatures that have appeared to breach the boundaries between the 'normal' and the 'abnormal' (Canguilhem, 2009) or between 'natural' biological organisms and 'designed' technological machines have been seen, at least since the nineteenth century, as monstrosities; the most famous of which is arguably Frankenstein's monster. Therefore, given that a key goal of synthetic biology is to synthesise "complex, biologically based (or inspired) systems, which display functions that do not exist in nature" (NEST, 2005) and thus to "engineer cells into tiny living devices" (Ferber, 2004: 158), synthetic biologists are finding themselves, as Craig Venter did, accused of playing God (ETC, 2007) and of treading in the footsteps of Frankenstein (van den Belt, 2009). Accusations of 'playing God' and comparisons to Frankenstein are clearly critical in intent, but where does the objection to creating life, that underlies these allegations, come from?

Creating life

Throughout human history, the likes of Copernicus, Newton, Darwin, and Einstein have challenged and changed our conceptions of the world we live in and our place within it (Goodfield, 1977). Such fundamental challenges continue to confront us as science advances and, with the continual development of new techniques to 'create' life, many of these challenges are now coming from within the life sciences. The potential for humans to act as 'creators' has raised concerns about 'playing God,' both in terms of the creation of human life through the likes of artificial insemination (Kline, 1963),

[84] Synthia is the name, first applied by the ETC group (2010) to the synthetic *M. mycoides* constructed by the J. Craig Venter Institute (Gibson et al. 2010).

and the creation of novel forms of life through genetic engineering (Goodfield, 1977). It is arguably into this latter category of creation that synthetic biology falls.

Perhaps surprisingly the notion of 'creating' life has not, however, always prompted the kind of controversy which now regularly accompanies advances in biotechnology (Schummer 2009). Rather, up until the early nineteenth century, the spontaneous generation of life out of inorganic or organic matter[85] was taken for granted, free of the contentions that accompany contemporary attempts to 'create' life. It was widely believed that under the right conditions life could be generated out of such substances as faeces, meat, hay, and rotting logs (Lennox 2001; Schummer 2009), or indeed out of the earth itself. As the first-century BCE Roman poet and philosopher Lucretius reportedly wrote in his didactic poem, *De rerum natura,* "with good reason the earth has gotten the name of mother, since all things are produced out of the earth. And many living creatures, even now, spring out of the earth, taking form by the rains and the heat of the sun"[86] (Lucretius quoted in Amicus 2011).

Such beliefs, supported by both scholars[87] and religious doctrine,[88] led to the development of a set of guidelines for undertaking the production of certain living beings. For example, the carcasses of cows were believed to create bees, the carcasses of horses were understood to produce wasps, and

[85] The notion of life arising from inorganic matter is called abiogenesis, while the notion of life arising from organic matter is referred to as hetergenesis.

[86] This poem was written to explain Epicurean philosophy to a Roman audience.

[87] Scholars such as Aristotle, Virgil, Ovid, Pliny, and Isidor of Sevilla for example supported the notion of the spontaneous generation of life. Aristotle, for example, wrote that "[a]nimals and plants come into being in earth and in liquid because there is water in earth, and air in water, and in all air there is vital heat; so that in a sense all things are full of soul. Therefore living things form quickly whenever this air and vital heat are enclosed in anything. When they are so enclosed, the corporeal liquid's being heated, there arises as it were a frothy bubble. The differentiae which determine whether the kind is more or less honorable are determined by the organization of the vital principle in the enclosure. And both the places and the enclosed material are causes of this organisation" (Aristotle, Generation of Animals III, quoted in Lennox 2001: 232-33).

[88] The Bible, the Talmud, the Upanishads, and other ancient texts and scriptures, contain stories of living organisms emerging out of inanimate matter. For example, in Exodus 8 of the Bible, two of the plagues, those of lice and frogs, are made out of dust and water respectively.

those of donkeys, beetles (Schummer 2009). Francis Bacon, in his posthumously published work *New Atlantis* (1627),[89] outlined an entire research program for the creation of novel plants and animals. Thus, given the widespread belief in, and acceptance of, such views, Schummer surmises that, "there were no basic philosophical, scientific, ethical, or theological objections to spontaneous generation or artificial creation of life. Indeed," he continues, "these were perfectly reconcilable with the biblical creation myth" (2009: 127).[90] Schummer extends his argument that manmade life is not inherently contentious by highlighting three unrelated, and relatively uncontroversial (at least in their own time), historical antecedents to the artificial creation of humanoids - ancient Greek and Egyptian automata, Kabbalistic golems, and alchemical homunculi.[91] Schummer (2009) maintains that none of these three traditions raised contemporaneous ethical or religious concerns as long as the work to produce them was not motivated by a desire to perfect divine creation by generating beings that were superior to natural humans.[92] For where the creation of plants and animals had not, and still did not, raise ethical or theological objections (given the wide acceptance of spontaneous generation), the creation of a creature with a 'rational soul,' a fully functional human, was open to a slew of theological objections including Satanism, tempting God, and hubris.

The scope for theological objection expanded however in the nineteenth century with the beginnings of Christian creationism, a belief system which

[89] Edited and republished by G. C. Moore-Smith (1900).

[90] In Genesis 1, the plants and animals are not created like Adam and Eve, but rather, upon the creator's fiat, they emerge out of earth, water, and air. Thus spontaneous generation and the artificial creation of life were viewed as being completely reconcilable with the bible (Schummer 2009).

[91] For a description and discussion of these humanoids see Lachman (2006), Lennox (2001), Schummer (2009), and de Solla Price (1964).

[92] However in the thirteenth century just such a shift in motivation began to drive the production of golems, a shift that was echoed in the sixteenth century production of alchemical homunculi. Indeed the homunculi texts (the recipes if you will) became famous because their authors all "considered the creation of homunculi the crowning power of alchemy in surpassing the power of nature and even that of the divine creator" (Schummer 2009: 130). Such claims, Schummer asserts, were the cause of some controversy.

arose out of a series of scientific developments starting in the seventeenth century (Schummer 2009). These developments included the emergence and prominence of the mechanical philosophy of natural theology[93] (which revived the notion of causal determinism[94]), the increasing use and rigor of experiments in scientific studies,[95,96] and perhaps most surprisingly, the

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[93] Mechanical philosophy, which was ultimately rooted in ancient Greek atomism, arose and gained popularity in the seventeenth century. It held that all natural phenomena could be explained in terms of matter, motion, and collisions between 'atoms,' the small imperceptible particles of matter which were thought to make up everything in the material world (de Solla Price 1964; Osler 2004). One of the first systematic, and most influential, accounts of mechanical philosophy was published by French natural philosopher Pierre Gassendi. Gassendi, a Catholic priest, detailed his view of mechanical philosophy in *Syntagma philosophicum* (1658). He believed that God had created a finite number of 'atoms' and had imbued them all with motion, and that these 'atoms' made up everything in the material world. He also asserted that all beings possessed a material, sensible soul (alongside an immaterial, immortal soul), which was composed of such 'atoms,' and that this material soul was transmitted from generation to generation through biological reproduction (Osler 2004). Gassendi, and those that followed his line of thinking, therefore believed that all 'atoms,' and thus all living beings, were ultimately connected back to primordial creation. As all phenomena could, purportedly, be explained through the motion of these 'atoms' under physical laws, all phenomena, past, present and future, could not be self-caused but must then be absolutely determined and linked to divine creation thus providing one of the pillars upon which creationism was erected (Schummer 2009).

[94] Causal determinism is a theological idea, which holds that any given phenomenon can be linked back to the primordial creation through a deterministic chain of events.

[95] Like mechanical philosophy, the increase in scientific rigor, played a role in the development of Christian creationism, but it also played a significant part in debunking spontaneous generation. Indeed, as experimentation became more rigorous, the standard list of organisms believed to arise from spontaneous generation shrank substantially, and continued to shrink as small mammals, insects, bacteria, viruses, prions, and self-sustaining molecular systems were systematically eliminated. Each organism that was removed from this list, following the determination of its reproductive mechanism, became, in turn, a candidate for primordial creation, bolstering the case for creationism. For many of the scientists involved in whittling down this standard list, including Louis Pasteur, the motivation behind debunking the idea of spontaneous generation was religious, as spontaneous generation had shifted from a banal reality, to a perceived threat to the fundamentals of Christianity. As such it was seen as essential that spontaneous generation be refuted in order to 'prove' that all life therefore must have been 'created' by God. Nevertheless, the question of whether spontaneous generation can, or does, ever occur has never been definitively answered. Rather, as candidates for such generation have become simpler, the line between life and nonlife has become increasingly blurred.

[96] See Huxley's 1870 Presidential Address to the British Association for the Advancement of Science for an interesting account of the inquiries, experiments, and scientific advances which led to the debunking of abiogenesis (Huxley 1893).

advancement of Darwin's theory of biological evolution[97] (Schummer 2009). All three of these scientific developments ultimately expanded the scope and importance of natural theology, especially within the Christian church, resulting in significant changes to the Christian value system. Where the creation of living beings had not previously been of religious concern, unless a 'rational soul' was involved, now the making of life at any level, including the chemical synthesis of organic compounds,[98] was open to scrutiny and accusations of 'playing God.'

Playing God

'Playing God' is subsequently a particularly laden accusation, having been employed over the years to critique a wide range of professions and situations. Teachers passing down grades to their students (Skinner 1939), medical teams who make decisions regarding transplant recipients (Harken 1968), the State's application of capital punishment (Gerstein 1960), and even Jane Austen's meddling character Emma (Shannon 1956) have all been charged with, or have faced their own personal concern with, 'playing God.' However perhaps the most common target in recent years has been biotechnology (Goodfield 1977; Howard and Rifkin 1977; Pollan 1998; Sale 1999). It should therefore come as no surprise that synthetic biology, as a branch of biotechnology with an explicit desire to create new forms of life, has, as the headlines that greeted the J. Craig Venter Institute's announcement show, also been subjected to accusations of playing God (Douglas and Savulescu 2010; ETC Group 2007). However, perhaps surprisingly, in synthetic biology as in all of these other

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[97] While Darwin avoided addressing spontaneous generation in public, many of his contemporaries, including Pasteur, saw in his work a clear path through evolution from spontaneous generation to the evolution of humans (Geison 2014). Thus, while today's creationists view Darwin's work as a threat to creationism, Darwin's theory prompted the development of creationism by linking spontaneous generation to the generation of humans. This link was taken as evidence that all living beings, and not just those with a rational soul, owed their existence to the primordial divine creation (Schummer 2009).

[98] As such, nineteenth century chemists also came under fire and suspicion as they strove to refute vitalism by systematically synthesising organic compounds.

situations, there is an argument that the charge of 'playing God' is not necessarily indicative of a religious opposition.

Grey (1998), Drees (2002), and Peters (2006) have each highlighted that both religious and secular groups raise the charge of 'playing God.' Grey claims, therefore, that rather than always being a religious argument, in a secular context the term is used metaphorically "to indicate that the consequences of an act are exceedingly serious or far-reaching and must therefore be considered with very great care," continuing that "the phrase may also be used to describe paternalistic or authoritarian decisions, often resented, made by individuals in positions of power" (Grey 1998: 335). Indeed, even some theologists, such as Peters (2003) and Dabrock (2009), contend that, despite the history outlined above, there are no principled objections of a religious nature against the making of new life forms, as synthetic biology aims to do.

Thus, rather than being an explicit religious argument, Davies et al. (2009) argue that the term 'playing God' acts as a symbolic expression of inexpressible concerns. Consequently it is potentially more interesting to shift the focus away from the religious wording of the term, which is easily dismissed by those without religious inclination, to look instead at the concerns it represents. 'Playing God' may be better understood, as Grey suggests, as a concern with the use of power, the making of decisions that affect others, and with "humans letting their power and knowledge exceed their caution" (Kirkham 2006: 176). Hence, despite Venter dismissing questions of 'playing God' as simply a result of scientific progress,[99] the concerns underlying this symbolic expression, as Kirkham (2006) and Grey (1998) stress, should not be ignored or dismissed.

Kirkham (2006) claims that the secular version of the term 'playing God' is 'vexing nature' and that the concerns that underlie both are essentially the

[99] He is quoted as saying, "Every time we understand a little more and get some command over nature, these terms come up. It's one of the consequences of making breakthroughs" (Sample 2010: 3).

same. For, as Ball (2010) and Grey (1998) indicate, nature and the natural are often held in high esteem by both religious and secular groups. Thus, it is often perceived transgressions against the natural order of things that encounter these objections. As bioethicist Arthur Caplan notes there is concern that synthetic biologists may be "manipulating nature without knowing where they are going" (Caplan quoted in J. Carey 2007: 40). Caplan also notes that, "while creating new life may not be playing God, it has revolutionary implications for how we see ourselves. When we can synthesize life, it makes the notion of a living being less special" (Caplan quoted in J. Carey 2007: 40). This statement from Caplan in turn raises a question; is a living being indeed special? And if the answer to this question is yes, what exactly makes it so?

Organisms and machines

Venter is quoted in the Guardian as saying, in regards to his team's success, "[i]t has definitely changed my views of definitions of life and how life works" (Sample 2010: 1). The questions 'what is life?' and 'what are the essential differences, if any, between the living and the non-living, the animate and the inanimate,[100] and organisms and machines?,'[101] that Venter's work raised not only for himself but for many others, have been around since at least the fourth century BCE. At this time, as shall be discussed in chapter six, Aristotle became the first person to attempt a general definition of life, by distinguishing it from non-life. He wrote, "[o]f natural bodies [that is, those not fabricated by man], some possess vitality, others do not. We mean by 'possessing vitality' that a thing can nourish itself and grow and decay"

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[100] Interestingly, the words 'animal' and 'animate' come from the Latin anima and the Greek anemos which mean breath (Canguilhem 2000).

[101] While similar, there are significant differences between these categories. The distinctions between living and non-living entities map onto those between the animate and the inanimate, but the same is not true for the distinctions between machines and organisms. Indeed, while all non-living entities are inanimate, not all inanimate entities are considered machines; think of a rock for instance. Furthermore, and arguably less obviously, not all entities that have historically been, and contemporarily are, considered to be, or treated as, machines are inanimate.

(quoted in Canguilhem 2000: 67). Since this time, attempts to address the above questions have often assumed the existence of a boundary between organisms and machines. Thus, rather than question the existence of such a division, much of the media coverage of Venter's 'synthetic' organism debated whether this assumed boundary had been transgressed.

Interestingly, this focus was in line with much of the early historical debate around the machine/organism divide, a debate that concerned what, and sometimes who, fell on either side of the division. In the fourth century BCE, for example, Aristotle argued that slaves, who he referred to as "animate machines," fell on the machine side of the machine/organism boundary. While in the seventeenth century Descartes more famously, though potentially less controversially, argued that all animals were machines (Canguilhem 2009). As shall be addressed in chapter six, Descartes held that the body, with its material parts, works like a machine while the nonmaterial soul, or mind, does not follow the laws of nature, but interacts with the body through the pineal gland. Thus his argument that animals were essentially reflex-driven 'animal-machines' was based on his notion that animals have no soul, and therefore cannot judge, understand, or feel pain and consequently do not qualify as rational beings under his famous dictum *Cogito ergo sum* (I think therefore I am) (Allen and Trestman 2014; Canguilhem 2009; Dawkins 2011). While Aristotle and Descartes' arguments no longer hold sway, having been motivated, according to Canguilhem (2009), by a desire to justify the exploitation of, in turn, slaves and animals, the notion that a machine/organism divide exists remained strong.

Indeed, in 1790 Immanuel Kant followed in the footsteps of Aristotle by dividing all things in nature into two categories, the inorganic and the organic[102] introducing the term self-organisation[103] as a way of characterising what it was that singled out organisms from other subjects (Keller 2008). Kant

[102] It is worth noting that this predates the formation of 'biology' as a distinct and separate field of science by a decade.

[103] In Kant (1987).

reportedly contended that an organism is "not merely self-steering, self-governing, and self-maintaining; it is also self-organizing. More, it is self-generating," thus it is both "*cause and effect of itself*" (Kant quoted in Keller 2008: 49). The emphasis here was very much upon the 'self' for it was the autonomy of the organism to perform these functions on or within itself, that Kant argued, in a similar vein to Canguilhem (2009) and Nicholson (2013) after him, set it apart from a machine, no matter how organised. Drawing on Kant then, Keller defines an organism as "a body which, by virtue of its peculiar and particular organization, is constituted as a 'self' - an entity that . . . achieves both autonomy and the capacity for self-generation" (2008: 49). Thus, while machines and organisms continued to be used as analogies for each other,[104] it was this concept of their different forms of organisation, self-perpetuated vs. externally determined, which prevented organisms from being confused with machines (Keller 2008).

The emergence of thermodynamics in the mid-nineteenth century however, saw the boundary between organisms and inanimate, physical systems become less clear as the existence of the boundary itself increasingly came into question. Thermodynamic experiments, such as that by von Helmholtz,[105] were used to argue that there was no longer any basis for arguing that organisms were governed by distinct processes (Keller 2008). Further efforts to disprove the existence of the boundary followed, such as moves to apply the concepts of "stability, equilibrium, and fixity (and later, of steady states) in describing features of biological regulation" (Keller 2008: 52) in order to assimilate organic systems with inorganic systems. However, the speculative and ambiguous usage of such concepts simultaneously left open the possibility that biology was, as Caplan's quote above suggests, something distinct, and the notion of a boundary between biological systems and physico-chemical

[104] See Nicholson (2013) for a discussion of such analogies.

[105] Von Helmholtz, one of the early proponents of the principle of energy conservation (Kuhn 1959), demonstrated the equivalence of animal heat and energy by showing that muscle tissue, in isolation, produces heat. An explanation of such heat that did not require the presence of a 'vital force' (Blaxter 1989).

systems survived. Indeed, the 1920s saw a drive to oppose thermodynamics' reductionism. For example, physiologist Walter Cannon attempted to bolster the argument for a clear divide through the introduction of the term 'homeostasis.' Homeostasis, Cannon hoped, could be used to differentiate "the kind of stability maintained by biological systems from simple physico-chemical equilibria" (Keller 2008: 61). Homeostasis then, like self-organisation before it, was used to signal the distinctiveness of organisms, and was largely successful in this endeavour until the rise of cybernetics in the 1940s (Keller 2008).

Keller writes that while there was a lot of focus on the relationship between organisms and physico-chemical systems during the nineteenth century, there was not much focus on the divide between organisms and machines. It was widely accepted that machines could be designed to self-regulate but, Keller argues, no links were made between biological self-regulation and its mechanical counterpart (2008). However with the end of World War II, and in the wake of the technological leaps that had been achieved as part of the war effort, cybernetics was born. According to Keller, the basic argument of cybernetics was that the "relation between organisms and machines was not merely analogous, but homologous: organisms *were* machines, and at least some machines could be organisms" (2008: 47). Accordingly, those within cybernetics held that, "it ought to be possible to build machines with the same self-organizing capacities as organisms" (2008: 47). Rather ironically cybernetics co-opted Kant's term 'self-organisation' to describe this program of work. Cybernetics then, like thermodynamics before it, held that no division between machines and organisms exists. Yet, rather than simply evidencing this through experiments, cybernetics aimed to create entities that breached the divide, thus proving that the notion of the divide's existence was untenable.

For twenty years efforts to create self-organising, communicative machine systems, which would, it was hoped, qualify as organisms, continued within cybernetics. However, due to its lack of progress, cybernetics fell out of favour within computer science and, in the 1960s, molecular biology took over the conversation on self-organisation (Keller 2008). With this shift, the efforts to breach the machine/organism divide continued, however such efforts were now predominantly driven from the organism side of the divide. Consequently, the conversation around self-organisation shifted at this time to focus on its role in the formation and emergence of stable patterns within low-entropy, non-equilibrium systems governed by nonlinear dynamics, the prime example being organisms (Eigen 1971; Nicolis and Prigogine 1977).

This focus on nonlinearity in far-from-equilibrium systems, continued to influence the work on self-organisation, as well as understandings of the origins of life, and thus the 'nature' of biological organisms throughout the 1970s and 80s. Charles Bennett, for example, wrote "dissipation has taken over one of the functions formerly performed by God: It makes matter transcend the clod-like nature it would manifest at equilibrium, and behave instead in dramatic and unforeseen ways, molding itself for example into thunderstorms, people and umbrellas" (1986: 586). The result of this conceptual shift was, therefore, a further assault on the notion of a machine/organism divide as, "life itself was reconceptualized as a self-organizing system, with the same kinds of properties that had previously been encountered in fluid dynamics and statistical mechanics" (Keller 2009a: 17). This reconceptualisation of the relationship between organisms and machines led in turn to the development of the science of complexity.

Complexity

The science of complexity arose in the late 1980s and 90s as an attempt to find a unified theory of complex systems, including both animate and inanimate systems. Much effort has, since this time, been expended in the search for such a theory, however the desired universality has largely proved elusive (Keller 2009a). Thus, while Kant's term, self-organisation, has come to refer to any complex phenomena arising out of random ensembles, such emergent patterns, though complex, continue to lack meaning. "Stripes, rolls, whirls, eddies are all phenomena indicative of complex, nonlinear dynamics; they are phenomena that can only be found in systems that share with organisms the property of being open, far from equilibrium, dissipative." However, Keller continues, "they still lack the properties that make organisms so insistently different from physical systems. Most notably, they lack function, agency, and purpose" (2009a: 27). Keller argues that such properties may therefore require a greater level of complexity than that which emerges spontaneously out of complex interactions between simple components. A level of complexity which some have termed organised complexity (Keller 2009a), and one that Nobel Prize winner Hebert Simon argued is complexity with hierarchical architecture (1962).

Yet despite such hypotheses, and despite decades of attempts, no satisfying account of the origins of life, or of life's organisation, yet exists. That is, despite decades of work, organisms cannot yet be fully explained using what we know of physico-chemical systems, thus they cannot yet be accounted for using the reductionistic approach synthetic biology adheres to. There is plenty of evidence supporting the notion that organisms can be explained in solely physico-chemical terms, but the explanation itself is incomplete. Perhaps then, Keller concedes, Kant was right, "perhaps the task is just too difficult - too large - for the mind to encompass" (2009a: 30). This position would leave open the chance that we may not ever be able to fully comprehend what makes life, life. Which subsequently raises questions regarding synthetic biology's practical and conceptual doability. Can we truly engineer life, in the manner synthetic biology aims to, if we do not full understand it? Furthermore this position, like all the attempts before it, fails to unequivocally put to rest the issue of whether or not a machine/organism divide exists.

Blurring the boundary

The history recounted above is replete with examples of organisms, and their characteristics, being reduced to and reclassified as physico-chemical processes or machine-like qualities, and of machines and their characteristics being reclassified as organic or life-like. Yet the results of such categorisations and analogies, like the results of experimental imitations of life, have never truly spanned the divide between the animate and inanimate. Loeb's (1912) famous sea urchins, produced through artificial parthenogenesis were, like babies born following In Vitro Fertilisation, undeniably animate. While Leduc's (1911) artificial cells, made using inorganic fluids and crystals were, like the products of modern Artificial Intelligence, undoubtedly inanimate.

However, Deplazes and Huppenbauer (2009) contend that, unlike such historical attempts, synthetic biology is actually spanning this divide. Through the use of both basic natural mechanisms and computers in the design of systems, Deplazes and Huppenbauer maintain that "synthetic biology as a whole approaches the borderline between living and non-living matter from both sides, the living and the inanimate" (2009: 56). Thus creating entities, like 'Synthia' and syn3.0, that "seem not to stretch but to transgress the borderline between organisms and machines" (2009: 62). As such, Deplazes and Huppenbauer argue that synthetic biology may well be the first endeavour to successfully blur this boundary, as "the aim of producing novel types of living organisms in synthetic biology not only implies the production of living from non-living matter, but also the idea of using living matter and turning it into machines, which are traditionally considered non-living" (2009: 56). This then helps to explain why Craig Venter's announcement made the waves it did.

Before 'Synthia' the discussion had been hypothetical, anticipating how we would classify such future entities, but with 'Synthia's' arrival, hailed as 'she' was as the "first artificial organism" (The Economist 2010), the 'future' had arrived and the machine/organism divide was under attack. It was therefore, in the wake of this shake-up that I was undertaking my fieldwork. Many of the synthetic biologists at the Centre were not convinced that 'Synthia' was as much of a game-changer as Craig Venter, or the media, would have you believe. However the hype that had accompanied 'her' unveiling did raise questions for these same synthetic biologists about how they themselves viewed and classified the 'products' of their discipline and their work. It is to the answers and internal debates that these questions generated that I now turn my attention.

Exploring the boundaries

How synthetic biologists refer to the 'products' of their work may seem to be a simple case of nomenclature, however, Deplazes and Huppenbauer suggest, such decisions have profound conceptual and philosophical underpinnings. They write, "[b]y calling their product an artificial or synthetic cell scientists are announcing that life no longer is only a natural process and feature. They point out that the phenomenon 'life' will be fully understood by scientists, and this understanding should enable the production of life" (2009: 61). Venter's claims around 'Synthia' are a perfect example of this with the artificiality of 'her' origins and 'parenthood' being arguably overstated in order to make this point. Referring to synthetic biology's products as synthetic/artificial/man-made organisms therefore suggests, according to Deplazes and Huppenbauer, that you see the creation of life as a purely replicable, mechanical process. Furthermore, they claim, "calling a genetically engineered bacterium a machine conveys a completely different message. It points out that these entities are controlled and produced by human beings who can dispose of them freely and that these entities are no longer part of the realm of nature" (2009: 62). Thus, they argue, classifying the products of synthetic biology as machines suggests that you view life, not just it's creation but all its processes, as designable, mechanical, and disposable.

And yet, as is evident in the announcement of syn3.0 (Clyde A. Hutchison et al. 2016), with its 149 mystery genes, even Venter admits to not yet fully understanding 'life.' Which, as discussed in chapter one, raises the question of whether life can truly be considered engineerable if the function of the parts is not fully understood. This gap in understanding, it should be stressed, is arguably a fundamental problem for the application of the engineering approach as it was laid out in chapter four. Genes whose functions are completely unknown (where it is not simply a case of 'we know what it does but not how it does it,' but rather 'we don't even know what it does') cannot be subjected to standardisation, characterisation, or abstraction. Thus despite a strong commitment to taking an engineering approach to biology, as discussed in chapter four the prevailing rhetoric of synthetic biology seems to be out of step with the reality of synthetic biology.

This rhetoric suggests that biological organisms are fundamentally no different to other inanimate, engineerable materials, and hence that the products of engineering endeavours in biology can themselves be thought of as engineered entities. However the question I shall be exploring below is, do synthetic biologists themselves see the products of their work in this way? Given their commitment to synthetic biology, the epitome of the reductionistic approach to biology, I initially assumed that the synthetic biologists at the Centre would uniformly reject the notion of a machine/organism divide. However, as this chapter outlines, the boundaries of life are problematic to say the least.

In *The Politics of Life Itself: Biomedicine, power, and subjectivity in the twenty-first century*, Nikolas Rose addresses this issue writing that "[o]ur very sense of what is or is not life, living, or alive is often exactly what is at stake in the politics of the present. A host of entities inhabit a transitional zone where their life-liness is precisely in question" (2007: 48). Rose is referring here to two specific kinds of liminal entities, those involved in reproductive technologies, such as sperm, ova, blastocysts, and embryos, and those that did not previously exist but rather are generated at the intersection of reproductive and stem-cell technologies such as stem cells and stem cell lines. Although he does not mention them, the products of synthetic biology, designed on computers and 'built' in the laboratory, would, it seems, fall within Rose's transitional zone. As Rose asserts, such entities highlight the philosophy of life embodied in individuals' ways of thinking and acting, and in the ways they differentiate between life and nonlife (N. Rose 2007). Thus, exploring the ways in which the synthetic biologists at the Centre classify the 'products' of their work, as I shall below, provides an insight into their philosophy of life, and thus into their take on whether biology is indeed engineerable.

Deplazes and Huppenbauer (2009), Latour (1987), Haraway (1997), Keller (2002), and Arthur (2009), all independently suggest that drawing a boundary between organisms and machines is an increasingly difficult and/or meaningless endeavour. Not surprisingly then, given the discipline's adoption of such a mechanistic approach to, and conception of, biology, many of the synthetic biologists within the Centre also expressed this viewpoint, as I expected. They told me, in a variety of ways, that they see no clear boundary between organisms and machines, but rather envision a grey area between the two.

> *I think there's no clear boundary. Because I've thought about this for a while, like where do you draw the line, right? . . . you can just keep decomposing the matter where you are, right? Like keep decomposing to the next level and then it's really tough to define what life is.*
>
> (Christian, doctoral student, biology)

> *I think that there's a big grey area as to . . . where a living system begins and a non-living system ends.*
>
> (Ryan, postdoctoral researcher, biology)

> *This distinction* [between machines and organisms] *will become much more . . . blurry than it is now.*
>
> (Grant, senior researcher, engineering)

Like many others within the Centre, Christian, Ryan, and Grant all expressed, in their own ways, doubts regarding the existence of a clear boundary between organisms and machines. For Christian, his qualms are underpinned by a belief in the mechanistic conception of the organism, that you can "*just keep decomposing the matter . . . to the next level*" until life is fully explained in physico-chemical terms. Whereas, in their descriptions of a blurry, grey mid-zone between machines and organisms Ryan and Grant appear to be implying that there is a difference between these two categories but that defining this difference and locating a clear division between them is difficult, and possibly increasingly so as synthetic biology advances.

For some of the synthetic biologists at the Centre, such as Simon, Lewis, and Trevor, it was within this grey area that they saw the 'products' of their discipline falling.

> *We're doing something that's in the middle between machines and life forms.*
>
> (Simon, doctoral student, biology)

> *I think* [a product of synthetic biology] *would be both* [an organism and a machine] *actually . . . it probably would just be a hybrid of the two.*
>
> (Lewis, doctoral student, engineering)

> *This machine will contain this biological system that you designed, and you also can have an interface between . . . this machine field and this living field, like . . . we have overcome the barrier between electrical side, the electrical field and the living organism field, the biology side.*
>
> (Trevor, postdoctoral researcher, engineering)

Yet, while these three synthetic biologists contend that it is difficult to assign their discipline's 'products' to either the machines or organisms category, the classifications they do assign to them subtly differ. While Simon asserted that synthetic biology's 'products' belong in the grey area located "*in the middle between machines and life forms*" being neither fully one nor the other, both Lewis and Trevor conversely saw them as *"both,"* being, much like the discipline itself, boundary spanning "*hybrid[s] of the two.*"

Others within the Centre similarly saw no clear boundary between machines and organisms but, rather than conceiving of a grey area, believed in an essential inanimate homogeneity between the 'categories.' For Peter, his belief in an essential homogeneity between machines and organisms was prompted by the observation that the enzymes in the cells he works with are "*the ultimate nano-machines*" rendering the cells themselves as simply the housing or 'factory' that contains a collection of such enzymatic "*mini-machines*," and the notion of a machine/organism divide, nonsensical.

> *Enzymes are the ultimate nano-machines. I mean . . . when you see how some of these enzymes operate in cells they are mini-machines, so therefore I don't see a divide, no. No.*
>
> (Peter, senior researcher, biology)

Like Peter, Grant also expressed a mechanistic conception of organisms, arguing that the "*simple organisms and bacteria*" they work with are not only looked at and treated as machines, but that they essentially are machines.

> *The way we are currently looking at simple organisms and bacteria is as machines. We try to get down to the mechanistic* [basis] *of those things and to get a level of understanding that allows us to treat them as machines, as things that we can on demand force to do things that they are not intended . . . to do in the first place. So yeah, that's what you do with a machine, right? You create something that can perform tasks for you, in a way that is reliable . . . A ribosome is what? It's a protein-producing factory that takes a blueprint at its entry and produces fantastic 3D fundamental units for the functioning of the cell. It's a machine, isn't it? Isn't that what a machine does?*
>
> (Grant, senior researcher, engineering)

For Michael however, the notion of an essential homogeneity between machines and organisms arose not from a recognition of machine-like qualities in organisms, but rather from a belief that all matter is inanimate.

> *There's no vital element of biological material . . . So this might be the final sort of death knell for vitalism . . . that everything is dead, that there is no life, that nothing is alive, that everything is dead. Everything's inanimate . . . there's no inherent difference in the matter that makes up me than makes up this computer.*
>
> (Michael, senior researcher, biology)

Michael's assertions that "*there is no life*" and "*everything's inanimate*" illustrate a consequence of synthetic biology's engineering approach previously discussed by Pablo Schyfter (2012). Drawing on Heidegger, and his notion of *Ge-stell*, Schyfter writes that in synthetic biology the focus on reducing living organisms to a combination of biological functions leads to the position that "[t]here do not exist living things; rather, there exist functions" (2012: 217). This mechanistic view of organisms, which is clearly evident in the quotes from Peter, Grant, and Michael, is an essential element of synthetic biology. Synthetic biologists are, after all, taking this mechanistic approach extremely literally. They are attempting to render the organisms they work with as collections of functions, or 'parts,' that can be linked together in order to produce an entity, which will behave in a predetermined and desired way, as Grant outlines above.

Michael is obviously demonstrating this same conviction, however I found Michael's emphatic rejection of vitalism and unequivocal acceptance of mechanism particularly striking. Not only did his answer display a complete lack of the uncertainty expressed by most of his colleagues, but also it was the only unambiguous response I received. Even Peter and Grant waivered in their mechanistic conviction as they tried to make sense of the 'products' of their work, but Michael did not. Given my expectations, it was not Michael's lack of uncertainty that surprised me, but rather, it was the doubt expressed by so many others that intrigued me.

Indeed, despite synthetic biology's adherence to an engineering approach, and the widespread, ostensible rejection of vitalism by those within the Centre, I repeatedly encountered the viewpoint that living entities possess something that sets them apart from machines. For some, such as Jessica and Martin, this led to internal conflict. They were uncertain whether or not to believe that the boundary between machines and organisms was indeed blurring, as they maintained, at times in spite of themselves, that in their minds such entities bear distinct differences.

> *I'd like to say it depends but then I guess it shouldn't, you know . . . If I say it depends that implies that you could have . . . this bacterium is a machine but this other one is not, you know, so what's the difference between them? Somewhere there's . . . is it a sort of grey*

area, is there a line? . . . I personally would not think of a cell as a machine . . . Like we can make it do things, we can use it in the same way as a machine but I wouldn't think of it as a machine, even though at the end of the day it's all like, you know, the same kind of chemical reactions going on and stuff, but I just . . . I wouldn't think of it like that . . . because it is derived from living material.

(Jessica, doctoral student, biology)

In my head I'm always like, yeah, that's a machine, that's an organism. I mean when you really think about it, it's pretty hard to define a boundary. But yeah, notionally, there's a machine, and there's a cell, or there's life.

(Martin, senior researcher, biology)

Here both Jessica and Martin demonstrate a conflict between what they know of biology, that it has "*the same kind of chemical reactions going on"* as machines, and thus "*when you really think about it, it's pretty hard to define a boundary"* and a deep-seated belief that life cannot be reduced to purely mechanistic explanations. For Jessica this conflict led her to want to answer the question '*do you think of the products of synthetic biology as machines, as organisms, as something in-between, or as something else entirely?*' with "*it depends*." She wanted to say that some organisms are machines but others are not, yet she acknowledges that it would be hard to clearly state the defining difference.

Max, another doctoral student at the Centre, likewise struggled with whether or not he believed the boundary between organisms and machines to be blurred.

I don't even know if it's a blurring of the boundary, I think it's just . . . the way our attitude towards it changes. But if you look at it kind of empirically, I guess, you either say, everything is a machine, or organisms are organisms. [Laughs] *I don't know if I would ever say a machine is an organism, so . . . Yeah. I think we want it to be that*

blurred because it helps us one, engineer it, and two, get useful applications out of it. Whether or not it actually is, I'm not sure.
(Max, doctoral student, biology)

Max claims here that he isn't sure whether synthetic biology is blurring the machine/organism boundary, or whether people's attitudes to machines and organisms are simply changing. In his claim that you either believe that a boundary exists and that therefore "*organisms are organisms*" or you believe there is no boundary, and thus "*everything is a machine*," Max has essentially outlined the fundamental difference between vitalism and mechanism, yet at this point Max claims that he isn't sure how he feels about these positions. However, after giving me this answer Max sat for a moment in silence contemplating what he had just said. He then gave me this long, but I feel enlightening, account of the internal conflict that underlay his uncertainty regarding the essential homogeneity of machines and organisms. He said:

Even if it functions as a machine . . . you could never erase the basic characteristics of a living organism. So the machine part of it could never mask . . . the basic living function . . . I do believe that because we're applying engineering by definition we must be creating a machine . . . it's got defined inputs, defined outputs, but as soon as that becomes somewhat variable you've lost the machine part. It becomes cyborg-like bacteria? I don't know! I don't know a good way of defining what it is I think about them. I just think that we need to treat them like machines in order to be effective synthetic biologists, but biology being biology,[106] *given a certain amount of time they are not machines any more . . . and they probably never will be but we have to treat them like they are in order to get what we want out of them . . .* [So] *they're a machiney-somethingy-elsey thing at the very beginning, but soon enough they just become organisms again . . . maybe if we knew everything about the cell and could tune it*

[106] Here Max is referring to biology's propensity to evolve and adapt.

perfectly it would stop being an organism and be a machine. Maybe for me being an organism has got to be the unknown as well, because as soon as something's knowable it's not necessarily life, in my opinion. In a weird way! It just becomes a sum of its parts, whereas everything at the moment to us seems like greater than the sum of its parts . . . whereas a computer never seems greater than the sum of its parts.

(Max, doctoral student, biology)

Like Jessica then, Max contends that it is the biological nature of organisms, which sets them apart from inanimate entities, even though such a view contravenes the accepted notion within synthetic biology, as expressed above by Michael, that no such division exists. Yet Max's account also highlights a conflict over how to classify the 'products' of synthetic biology's endeavours. A conflict others within the Centre also acknowledged.

The complexity of classifications

Above, Max clearly struggles to clarify his thoughts about classifying the products of synthetic biology both to me, and to himself. For, while he states that, *"because we're applying engineering by definition we must be creating a machine,"* he sees this state as unstable. By his reckoning synthetic biology 'products' start as *"machiney-somethingy-elsey thing[s],"* but as their biological nature is expressed they become "*cyborg-like bacteria"* and then "*soon enough they just become organisms again."* This instability of classification is also addressed by Deplazes and Huppenbauer who write that the evolutionary capability of synthetic biology products "raises the question whether in subsequent generations, at a point when new structures and features have evolved, their origin should still be considered artificial or whether the 'processing by evolution' would render them natural" (2009: 60). This uncertainty highlights the complexity that lies in classifications of this sort. When you are designing 'products' using a computer, which will be 'built' using standardised, albeit, biological 'parts,' to fulfil determined, desired outcomes, which are ultimately reliant on your 'product's' biological, and at least partially unknown capabilities, how do you classify the resultant 'product'?

What is life and what is a machine?

In chapter four, I discussed the way in which the synthetic biologists I studied were embracing an engineering approach to biology, with its drive to design and build controllable, predictable organisms which will perform pre-determined, predictable tasks. Given this approach to biology and the commitment of those within the Centre to applying engineering discourse and methods to biology, what, I wondered, does this mean for 'life'?

Evelyn Fox Keller writes, as I quoted in chapter one, that "the question 'what is life?' is a historical question, answerable only in terms of the categories by which we as human actors choose to abide, the differences that we as human actors choose to honor, and not in either logical, scientific, or technical terms. It is in this sense that the category of life is a human rather than a natural kind" (2002: 294). I would argue that a similar case could be made regarding the question 'what is a machine?' As such, rather than debating which category the 'products' of synthetic biology 'really' fit into, I am more interested in examining the conceptual categories the synthetic biologists at the Centre are creating, and the differences they are choosing to honour when considering their discipline's 'products.'

As outlined in the quotes above, while most of the synthetic biologists at the Centre saw no clear boundary between machines and organisms, and some of them saw their products as hybrids or boundary-transgressing entities, others resisted the notion that the entities they are producing are machines. This could be due, in part, to 'machine' being, as Janet (senior researcher, biology) claimed, a "*rather loaded term.*" However, the quotes above and below from members of the Centre suggest that this resistance may also be linked to an assumption that there are certain characteristics of machines that synthetic biology's 'products' do not yet possess, and certain characteristics of organisms that they have not yet shed.

Honoured differences

In the lengthy quote above from Max, and in the question that followed from Deplazes and Huppenbauer (2009), the distinction that is being honoured is that between the artificial and the natural. In discussing whether evolution can, or inevitably will, turn an artificial lab-made entity into, or back into, a natural entity Max, and Deplazes and Huppenbauer, are placing these characteristics on either side of the machine/organism divide. Machines are, according to this form of classification artificial, while organisms are natural. Yet as Max addresses, such a classification in synthetic biology is unstable. Despite efforts to design and engineer the cells as machines, their biological ability to evolve and mutate can override and disrupt their engineered qualities. The instability of the artificial verses natural classification, and the difficulty of applying it to synthetic biology's products, was also addressed by Hayden, who said:

> *It's really hard to say if now an organism that has been heavily modified is still life, it's not life anymore, it's like artificial life, organic machine. I don't know . . . I mean . . . it's life modified . . . to work for us.*
>
> (Hayden, doctoral student, biology)

While Hayden, like Max, is uncertain how to ultimately classify the 'products' synthetic biology produces using the categories of machine and organism, he seems to find more clarity in defining their purpose. Such products are, he says, "*life modified to work for us*." Jessica also made such an appeal to the 'product's' purpose as a form of classification while also drawing a distinction between the artificial and the natural. Yet unlike Max and Hayden, she is not only referring to the engineered cells as potentially artificial, but also the environment within which they are produced and interact.

> *I think of these as cells that are only ever going to be used in the lab or in industry, I don't think of these as cells that are ever going to interact with anything in the real world. So in that sense I guess I would think*

> *of them as machines. I think of them as I guess somewhat different to, you know, like something I see out there.*
>
> (Jessica, doctoral student, biology)

As Jessica stresses, for her, the 'artificial' environment of the laboratory or industry, and her belief that the cells she makes and works with will only ever interact with other artificial things, renders them machines. This is in contrast to cells that are "*out there*" interacting in "*the real world*." Here the "*real*," 'natural' world is seen by Jessica as separate from the artificial world of the laboratory and industry. Yet it is not so much the perceived boundary between science and nature that Jessica is honouring in her model of classification but the purpose to which the cells are being put. That is, for Jessica the distinction between the cells produced by synthetic biology and those "*out there*" is that the synthetic biology cells have an artificial, human-determined purpose, and artificial, human-determined interactions, while those in the "*real world*" do not.

This foreshadows the division between mechanism and vitalism which shall be discussed in detail in chapter six, whereby mechanism holds that causation is externally determined, while vitalism maintains the notion of self-causation (Lash 2006). It would also seem that Jessica is adhering to a mechanistic conception of the organisms she, and others, work with and 'create' within synthetic biology, but is reluctant to apply this conception to 'wild' organisms out in the 'real' world. Such a position provides evidence for Deplazes and Huppenbauer's claim, quoted above, that classifying a synthetic biology 'product' as a machine indicates that they are "no longer part of the realm of nature" (2009: 62).

A further difference honoured in the attempt to draw a distinction between machines and organisms and classify synthetic biology's products as one, the other, or both is the distinction between understood, predictable, and controllable entities and entities that lack these qualities. Janet, like Max, Hayden, and Jessica, also struggled with how to classify the 'products' of synthetic biology, but unlike these others it wasn't a distinction between the natural and the artificial that Janet called upon. Rather, Janet determined that the 'products' of synthetic biology are not well enough understood, nor well enough controlled, to fulfil the requirements to be considered engineered machines.

> *I feel like* [referring to a 'product' of synthetic biology as an] *engineered machine sort of feels like you understand . . . enough about it that you can predict what it will do, and you don't in any way feel like it's not controllable.*
> (Janet, senior researcher, biology)

This echoes a sentiment Max expressed above when he suggested that if a cell could be tuned perfectly, if it was completely knowable and known, and thus if it was simply the sum of its parts, then it would no longer be 'life.' Life being inherently, by Max's estimation, "*greater than the sum of its parts*." Should these conditions be met, then, in Max's mind, a cell "*would stop being an organism and be a machine*." So, by this rationale, syn3.0, which still defies full understanding, is alive. Should Venter and his team succeed in connecting the 149 mystery genes to defined functions however, this would render it 'known,' and its 'lifelihood' may be called into question. Nevertheless, by Max's reasoning, as long as syn3.0 still mutates and evolves (the "*biology being biology*" he mentioned), it would resist control and would remain "*greater than the sum of its parts*" and thus it would not yet qualify as a machine. For Max, then, it is the biological nature and the unknown qualities of synthetic biology's 'products' that set them apart from machines. Whereas for Janet it is their lack of predictability and controllability, and for Christian and Jessica, quoted below, it is the dearth of design in their construction.

> *I guess that's about designing DNA, right, . . . that's where my definition looks like it's lying. I don't think 'Synthia' is that revolutionary because they didn't really design anything, they just reconstructed. So for me . . . that's not really that revolutionary, whereas if they actually did design it from scratch, . . . treating it like*

chemistry, I want this membrane, that structure, that type of ER,[107] *proteins, and polysaccharides . . . when we get to that point maybe it really is like a machine.*

(Christian, doctoral student, biology)

By Christian's reckoning synthetic biologists would need to be able to design and build an organism piecemeal from 'the ground up' before it could truly be considered a machine. Jessica also honoured this difference in her conceptual categories of machines and organisms, but unlike Christian, Jessica saw Venter's work as a significant step towards achieving designed, engineered, biological machines.

So a natural organism is clearly different from an engineered machine, just in the sense, you know . . . we didn't design it . . . [but] *it's a difference in degree not in kind . . . If you think of the kind of stuff that Craig Venter's doing, you know, if you can actually make like an artificial cell then that is clearly a lot closer to something like an engineered machine than what we've previously seen.*

(Jessica, doctoral student, biology)

The quotes within this chapter from Jessica also point towards an internal struggle over how to classify synthetic biology's 'products.' Jessica struggled with the idea of organisms being machines, and contended that she definitely sees the cell as being essentially different from inanimate machines, but, when she started to think about building them, she found herself seeing these cells as potentially machine-like. Others such as Sara, were also conflicted, feeling comfortable with the idea that simple organisms are no different from machines, but more hesitant to extrapolate that view to more complex organisms. When I asked Sara whether or not she perceives a difference between something that is a biological organism and something that is a designed machine, she responded:

---

[107] Endoplasmic reticulum.

> *It kind of depends on the organism!* [Laughs] *Because if it's just like E. coli that you can . . . program to make something for you and you have a machine making something for you . . . there is no difference. But it kind of depends, as I was saying, on the organism because, where do you stop then?*
>
> (Sara, doctoral student, engineering)

Sara's question, "*where do you stop then?*" highlights her belief that you would need to stop somewhere, that not all organisms can be thought of as machines. This is perhaps because simple organisms, such as *E. coli,* more readily fit within Sara's conceptual category of machines than do more complex organisms. Yet as the following quotes show, for others within the Centre, even these same simple organisms display enough characteristics and differences that are honoured in their definitions of life to make thinking of them as machines untenable.

> *You could argue that if a bacteria has been engineered so that it only exists for our own purpose then it's a machine instead, but I don't think so because to get* [the bacteria] *to do that . . . you still have to get it so it wants to live and replicate. . . . So maybe they should change iGEM to iGES, so Internationally Genetically Engineered Slaves. That's more applicable really than Internationally Genetically Engineered Machines.*
>
> (Martin, senior researcher, biology)

> *Even though we may create the most well-defined synthetic biology application bacteria, whatever, within three rounds of division that might not be the same organism, and I think the fact that we can't control it to that extent makes it not a machine. . . . I also believe that machines theoretically can become not machines, in the fact that in a purely hypothetical universe they may develop artificial intelligence, at which point that's no longer a machine to me because it's got free will.*
>
> (Max, doctoral student, biology)

Unlike the previous quotes which have addressed the characteristics honoured in the classification of 'machine,' both of the above quotes, and the one below, address characteristics honoured in definitions of life and thus of organisms. Such characteristics include self-replication, free will, a will to live, and the ability to evolve. The persistence of these characteristics within the 'products' of synthetic biology are as instrumental in leading these synthetic biologists to define them as organisms, and to differentiate them from machines, as their lack of machine characteristics such as controllability. Interestingly though, and in contrast to most of the members of the Centre who spoke of which characteristics their products would need to shed or gain to transgress the machine/organism boundary by becoming more machine-like, Max speaks here of what characteristics machines would need to gain in order to do the same from the opposite direction. Also of note within these quotes is Martin's comment that it might be more appropriate to classify the products of synthetic biology as slaves rather than as machines. As the following quote from Hayden, regarding the 'products' of synthetic biology shows, Martin was not alone in making such a statement.

> *I would put them more on the life* [side] . . . *but that doesn't mean it can't be used as a machine . . . you know, I don't think there's any problem exploiting some kind of life forms to do our bidding. It sounds bad but . . .* [laughs] *I mean I'm not saying we should enslave other humans but, you know . . . we could enslave bacteria, I'm totally OK with that!*
>
> (Hayden, doctoral student, biology)

Without getting distracted by a discussion of the ethics of enslaving another living entity, I do wish to highlight the resonance between these two synthetic biologists arguing that, what some see as biological machines, should be thought of as slaves, and Aristotle's argument that human slaves should be thought of as machines.

Like Max, both Martin and Sam determine that the products of synthetic biology retain too many of the characteristics they assign to the category of 'life' to be considered machines and thus they resist consigning them to the category of 'machines.' However where Martin jokes that iGEM should be renamed iGES, Sam considers the potential for a novel classificatory category for the products. Could they be considered artificial or manmade organisms, as the headlines around 'Synthia' suggest, rather than just being lumped in with other 'natural' organisms?

> *They are all organisms. Yeah, I mean I wouldn't necessarily see it as a machine, you may have engineered it to perform a specific task but this is where you sort of get into biology having its complexities that you don't have in a lot of other machines, because . . . presumably it would need to self-replicate, it would need to take in some sort of energy source. Well, you can say that about a machine. But . . . presumably it will evolve as well. So . . . I personally would consider that to be an organism, whether it's what you'd call an artificial or manmade organism or not is a completely different matter, because again you're getting into different stages of grey.*
> (Sam, postdoctoral researcher, biology)

Restrictive categories

Olma and Koukouzelis write, "if our existing categories increasingly turn out to be insufficient in dealing with the way the world becomes, is it legitimate to try to look for different ones?" (2007: 1-2). This question strikes at the heart of the internal classificatory conflicts experienced by some of the synthetic biologists at the Centre. Those who claimed that their 'products' fell into a 'grey' area between machines and organisms, or who claimed their 'products' as hybrids, were searching around for a new category having found the existing ones insufficient. The quote from Sam above shows a tentative suggestion that a new category might be required to account for the grey area synthetic biology finds itself in, but it is a potential that he shied away from exploring. Others at the Centre, such as Christian, were more forthright. Referring to the future products of synthetic biology Christian said:

It will be like a tree of life, but like massive, you know? So I think just from that, having that bit of technology I think it's going to . . . explode . . . the amount of diversities you're going to get. . . . But yeah, I think it would be kind of like a new form of life, which is kind of weird. But whether people would . . . class it as life, it's a difficult one to say.

(Christian, doctoral student, biology)

For Christian, the categories of machines and organisms, and even the category of life, are insufficient to hold synthetic biology's future 'products,' which, he maintains, will be a new form of life, necessitating an expansion of the classic tree of life. This brings to mind the work of designer Alexandra Daisy Ginsberg, whose piece *The Synthetic Kingdom* (figure 8) depicts the tree of life with a new branch, "Synthetica," attached to contain synthetic biology's products.

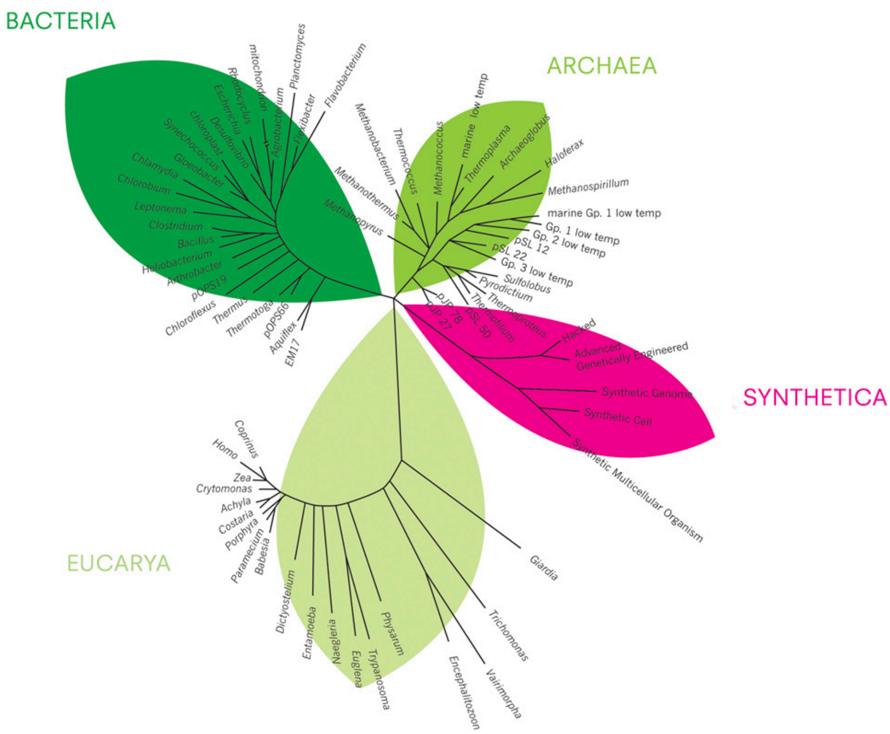

Figure 8: *The Synthetic Kingdom* by Alexandra Daisy Ginsberg (2010)

Ginsberg produced this work to provoke discussion of synthetic biology's drive to bring engineering and design into nature and to raise questions about how we can make sense of engineered life (2010). A large canvas bearing *The Synthetic Kingdom* hangs on the wall of the Centre's upstairs open plan office where, despite Ginsberg's intent, I encountered individuals debating the placement of Ginsberg's hypothetical "Synthetica" branch but never its inclusion in the tree which, it seemed, was taken for granted. Lewis however could be said to have taken it a step further than even Ginsberg, questioning not the inclusion of 'Synthetica' in the tree of life, but the sheer existence of the tree of life.

Like Christian, Lewis also saw the existing conceptual categories as limiting. However his objections lay not only with the categories of 'machine' and 'organism.' Lewis viewed the concept of the tree, itself a conceptual creation, as prohibitively rigid. Especially when it is used as an arbiter of what entities can and should be produced. While complaining about critics of synthetic biology who invoke the tree of life in order to protest potential entities which might span the machine/organism divide, Lewis said:

> *It's like, 'oh we can't do this, you know, it will really mess with the tree.' It's like, the tree doesn't fucking exist!*
>
> (Lewis, doctoral student, engineering)

Underlying Lewis' forceful opposition to the tree of life is the recognition that, as Keller wrote regarding life, such categories are human rather than natural in kind. Yet the critics Lewis is objecting to are those who perceive the tree as natural and thus as an entity to be defended rather than a conceptual tool to aid understanding.

Hayden likewise noted that, despite the human drive to categorise things, classifications do not work well in biology, as "*nature doesn't really need them*."

> *I know that people need those classifications . . . It happens for everything but for biology in particular definitions really don't work, because you know, nature doesn't really need them. . . . So I mean it doesn't surprise me that now we don't know if what we do is a*

> *machine or a life form . . . I think it's really important that everybody knows that we're doing something that's in the middle between machines and life forms, but that doesn't mean that then you have to decide which one it is, you can just say, OK, we're doing something in the middle, it's interesting, let's do it.*
>
> (Hayden, doctoral student, biology)

However, while rallying against the drive to categorise everything, Hayden simultaneously asserts that, "*it's really important that everyone knows that we're doing something in the middle between machines and life forms*." Thus suggesting that the 'products' of synthetic biology fall into the grey area between machines and organisms discussed above, and that the existence of this grey area needs to be noted and recognised. This itself suggests a form of classification, albeit classification outside of the existing categories of machines and organisms. Furthermore, by claiming that the products of synthetic biology are neither machines nor organisms but rather fall somewhere in the middle between these poles, Hayden is asserting that synthetic biology is already breaching the machine/organism divide by producing boundary spanning entities. This brings us back to the hybrid, grey zone that many of the members of the Centre assigned synthetic biology's 'products' to. Yet in light of the above discussion regarding classification, I wish to suggest the possible need for a hybrid conceptual category to inhabit this grey zone.

A hybrid category?

As discussed previously, although synthetic biologists are taking their mechanistic approach to biology literally, by treating organisms as collections of functions, 'parts' which can be linked together in order to produce entities that will behave in predetermined and desired ways, there is a lot about these organisms that is not controlled. After all, the 'products' synthetic biologists are attempting to 'design' and 'build' are, despite the engineering rhetoric and approach, reliant on the biological capabilities of the organisms themselves. Capabilities that is, which neither are, nor indeed could currently be, designed, built or controlled. This is the biological ignorance, and the limits of mechanism and reductionism which Bergson (1983), Greco (2005), and Canguilhem (2009) were referring to, and which many of the synthetic biologists at the Centre were aware of.

Thus, synthetic biologists ultimately only design and 'engineer' a very small part of any 'product,' and yet they are reliant on the whole of it, the whole cell or organism, to perform its desired task. In synthetic biology the 'parts' of the construct that are not designed, which are not standardised, categorised, bioparts, are referred to as the chassis. This mechanistic term hides the fact that the chassis itself is not just a structural scaffold for the 'product' to be built upon, but rather contains all of the cellular components necessary to keep the cell alive and functioning, and thus performing whatever task it has been 'designed' to perform. Yet, as syn3.0 so clearly demonstrated, we do not currently understand all of this componentry. Furthermore, as discussed above, despite decades of work, organisms cannot yet be fully explained using what we know of physico-chemical systems (Keller 2009a). Thus they cannot, at least as yet, be built completely from the 'ground up' using physico-chemical parts.

Accordingly, despite the Centre Director Alan's beliefs that "*we don't need to know how it works, we just need to know the inputs and outputs*," and that synthetic biology only needs to find, as he puts it, the "*islands of stability in an ocean of chaos*," synthetic biology is reliant on such unknown workings and oceans of chaos. Without these, the synthetic biological 'products' will not 'work.' Nevertheless, these 'products' are not indistinguishable from 'natural' organisms either. Their stripped down chassis, standardised parts, and industrial purposes set them apart from the organisms from which they were derived, even though they rely on, and maintain, their biological functions.

This brings to mind the wave-particle duality. The principle that addresses the inability of the classical concepts 'particle' and 'wave' to fully describe the behaviour of quantum-scale objects, the most commonly considered being light. Light is well known to be both a particle and a wave, exhibiting properties of both, a situation which led Einstein and Infeld to write:

> "But what is light really? Is it a wave or a shower of photons? . . . There seems no likelihood of forming a consistent description of the phenomena of light by a choice of only one of the two possible languages. It seems as though we must use sometimes the one theory and sometimes the other, while at times we may use either. We are faced with a new kind of difficulty. We have two contradictory pictures of reality; separately neither of them fully explains the phenomena of light, but together they do!" (1967: 262-63).

While there are some quite obvious differences between the phenomenon of light, and the 'products' of synthetic biology, I would argue that, as discussed above, such 'products' also fall between two classical categories, machines and organisms. Not sitting solely in one nor the other but rather requiring the explanatory power of both. This, as Einstein and Infeld put it in regards to light, is a difficulty. However, while they concede that, at first sight, the wave and particle theories are irreconcilable, they also argue that "[s]cience forces us to create new ideas, new theories. Their aim is to break down the wall of contradictions which frequently blocks the way of scientific progress. All the essential ideas in science were born in a dramatic conflict between reality and our attempts at understanding" (Einstein and Infeld 1967: 264).

Thus perhaps, as Deplazes and Huppenbauer (2009) contend, synthetic biology really is creating boundary spanning entities, and such entities will ultimately force us to create new ideas and new theories to categorise and understand them. Just as light is understood to be simultaneously both a particle and a wave,[108] so too may the products of synthetic biology come to be understood as being simultaneously both a machine and an organism. A situation that may, ultimately, necessitate the formation of a hybrid conceptual category to contain such entities. A boundary spanning category

[108] Something that was captured, for the first time recently (Piazza et al. 2015).

that is, to account for the boundary spanning products of a boundary spanning discipline.

However, for some within the Centre such hybridity is only an intermediate step. The ultimate goal being the creation of synthetic biology 'products' that completely breach the machine/organism divide, becoming indistinguishable from machines. While the achievement of this goal, these individuals argue, is simply a matter of time.

Not if, but when

As indicated above, several of the synthetic biologists at the Centre expressed views on the characteristics a synthetic biology 'product' would need to possess in order to stop being an organism, at least in their minds, and thus fully transgress the machine/organism boundary. The aggregate working definition of the 'category of life,' of those at the Centre, thus appears to encompass entities that reproduce, self-repair, evolve, and exercise free will, among other potentialities. Whereas the 'category of machine' implies, for these scientists, the possession of features including being well understood, controllable, stable, reliable, and designed and built from 'scratch.' Several synthetic biologists at the Centre echoed Max's comments that, due to the biological nature (the "*biology being biology*") of the organisms they work with, these organisms resist efforts to endow them with these characteristics. Nevertheless some, such as Christian and Jessica, see it as only a matter of time before they will be able to achieve this goal, thinking in terms of *"when"* rather than 'if' *"we get to that point."*

David, who shared the perspective that it is only a matter of time before synthetic biology's products can truly be thought of as machines, was perhaps the most excited about this prospect, telling me:

> *I'm really looking forward to ten, fifteen years down the line when we're starting to make these really complex machines, putting together several devices to make systems and then seeing what fireworks come out as a result, that's going to be a fantastic few years to be around. But it's a fun little stepping-stone for now.*
>
> (David, doctoral student, biology)

Grant, the most experienced engineer in the Centre, was likewise optimistic about the potential for synthetic biology to endow their 'products' with engineering characteristics. For him it was all about following a rational, engineering approach, an approach that, he argues, has seen technology progress in leaps and bounds since the industrial revolution.

> *We're dealing with things that during billions of years have been . . . mixed and matched, tinkered around, changed, evolved, to be more and more and more efficient, and . . . when did we start to engineer . . . what we call complex systems? When was the industrial revolution? Put that in perspective with the millions of years we have behind us and you still see that using rational approaches and . . . I would like to say engineering approach, we are not that bad at engineering stuff. We are very far from what biology has come up with during those billions of years but . . . if you look at the way things evolve and technology efficiency increases every year, well I bet you that in a few decades we will be quite far. . . . We're not as good as biology but we are trying to get there.*
>
> (Grant, senior researcher, engineering)

Grant suggests here that the ultimate goal of engineering is to be "*as good as biology,*" and surely being able to design, build, and control biological entities using rational approaches, would be a fair indication that this goal has been reached. However, as discussed both here and in chapter four, and as is indirectly acknowledged by Grant, this is not yet where synthetic biology is.

Nevertheless, the notion that it is simply a matter of time before the 'products' of synthetic biology possess the characteristics that would define them as machines, or as being indistinguishable from machines, also arguably owes a lot to the commitment to the engineering approach discussed in chapter four. As, through their attempts to apply both the engineering design cycle and the concepts of standardisation, abstraction, and decoupling, the synthetic biologists at the Centre are striving to endow their 'products' with these characteristics. Thus it is no surprise that members of the Centre, such as David and Grant, believe this goal is achievable. Yet, as clearly outlined above, there were others who were not so sure, adhering as they did to the notion of a machine/organism divide. Was this adherence due to humility, a desire to avoid the sort of limelight Craig Venter had been thrust into when he claimed to have breached the boundary? Or were they displaying an underlying, and unacknowledged, adherence to vitalism?

Vitality, complexity, reductionism

Michel Foucault wrote in his introduction to Canguilhem's (1989) *The Normal and the Pathological*:

> "the living being involves self-regulation and self-preservation processes; with increasing subtlety we can know the physico-chemical mechanisms which assure them; they nonetheless mark a specificity which the life sciences must take into account, save for themselves omitting what properly constitutes their object and their own domain" (1989: 18).

While this assertion that, in order to protect their academic domain from being subsumed within physics and chemistry, life scientists need to maintain the existence of a specificity of life, makes perfect sense for biology, it makes less sense for synthetic biology. Synthetic biology has, after all, embraced mechanism to such a degree that, as a discipline, it is striving to apply an engineering approach to biology in order to design and build biology in a modular fashion, much as any other engineered product would be designed and built. Thus synthetic biology's academic domain is not threatened by seeing organisms as machines; rather their entire approach is reliant on biology being machine-like. Thus, given their general commitment to this approach, why do so many of the members of the Centre assert that organisms cannot be thought of, treated as, nor equated with, machines?

Canguilhem writes that "the term *vitalism* is appropriate for any biology careful to maintain its independence from the annexationist ambitions of the sciences of matter" (2009: 60). Given the assertions of some of the synthetic biologists at the Centre that organisms are distinct from inanimate matter, one possible explanation is that these synthetic biologists are vitalists. I doubt anyone at the Centre would welcome the label of 'vitalist,' though there are, in some of their responses, grounds for exploring whether Canguilhem's form of vitalism is appropriate. Unlike traditional vitalists, who strove to prove that organisms possess a 'vital force' lacking in inanimate entities (Bechtel and Richardson 1998; Mayr 2002), Canguilhem conceded that such a take on vitalism may well appear to today's biologists to be merely an illusion of thought. However he also notes that, unlike other debunked scientific theories[109] vitalism continues to require refutation and debate.

Canguilhem refers to this as the vitality of vitalism and argues that, "the rebirths of vitalism translate, perhaps in discontinuous fashion, life's permanent distrust of the mechanization of life. In them we find life seeking to put mechanism back into its place within life" (2009: 73). Drawing on Canguilhem's work, Monica Greco (2005) consequently argues that it is vitalism's position as a form of resistance to reductionism that accounts for its vitality. For despite its questionable approach to biology, it has served an important role in the history of biology as a counterpoint to excessive reductionism and mechanism. Bergson made a similar point in 1911 when he wrote that, "the 'vital principle' might indeed not explain much, but it is at least a sort of label affixed to our ignorance, so as to remind us of this occasionally, while mechanism invites us to ignore that ignorance" (1983: 42).

[109] For example geocentricism, the idea that the Earth is the centre of the Universe and the planets revolve around it.

As discussed previously, within the Centre I encountered a lot of uncertainty regarding the classification of synthetic biology's 'products,' and much of this uncertainty was fraught with the kinds of doubts Canguilhem would ascribe to vitalism. For example, there were doubts over the extent to which organisms could be reduced to physico-chemical components and mechanistic explanations, and an awareness of how much we do not yet understand about the origins and organisation of life. Indeed, as I have outlined above, only one synthetic biologist at the Centre claimed to see absolutely no difference between organisms and machines. Whereas most struggled with defining the products of their work. Many believed that by applying an engineering approach and engineering methods, and by creating organisms that would serve designed and desired functions, they were essentially creating machines. However for some, such as Max, this line of reasoning, which they outlined themselves, did not dissuade them from their belief in the essential differentiation between machines and organisms.

> *I'd like to believe that everything is a machine that, you know, it's a tool . . . I'd like to believe that. But I don't believe it.*
> (Max, doctoral student, biology)

Why then did Max not believe it? Canguilhem might argue that Max, and those like him, are essentially vitalists. And yet, they were more likely to attribute biology's uniqueness to, what Greco (2005) sees as the modern day equivalent of Canguilhem's 'vitalism,' complexity. As Greco writes, "complexity can be read as constituting an intellectual demand, an ethical imperative, that is not dissimilar to what Canguilhem addressed through the theme of the 'vitality of vitalism.' Complexity expresses the demand that we acknowledge, and learn to value as the source of qualitatively new questions, the possibility of a form of ignorance that cannot simply be deferred to future knowledge" (Greco 2005: 24). Not one member of the Centre invoked 'vitalism' as an explanation for why they perceived a difference between organisms and machines, but several, such as Jessica, raised the issue of complexity.

> *It's hard to say whether there's something fundamentally different about a living organism compared to a machine because it's just . . . so complex at the moment we don't quite understand yet how it works, you know, with a machine we understand how it works, with an organism we don't and we don't quite know yet whether . . . when you look at the fundamental processes it's just kind of like a machine or whether it's actually so complex that not in a thousand years would we ever be able to create something like that from scratch.*
> (Jessica, doctoral student, biology)

Greco argues that as vitalism has fallen out of favour new theories and concepts, such as complexity, have taken its place as signifiers of our ignorance regarding, and attempts to explain, the origins and organisation of life without resorting to simple reductionism. Such concepts have abandoned the metaphysical aspects of vitalism but retain its ambiguity. As such, perhaps the persistence of doubt over the applicability of the mechanistic conception and treatment of the organism is due to an acknowledgement of the inherent complexity in life. These doubts seemed stronger in those with a biology background than those with an engineering background, which may be due to their differing knowledge of, and experience of working with, biology.

As discussed in chapter three, there is a vast difference in the knowledge base of synthetic biologists who hail from biology and those who hail from engineering. Many of those from engineering have little or no training in biology and thus are surprised to discover how difficult it is to engineer. As engineer Jack Schonbrun is quoted as saying, in regards to synthetic biology, "[t]he synthetic part is easy, it's the biology part that's confounding" (Gardner 2013). Thus, perhaps those hailing from engineering are less aware of the gaps in the physico-chemical explanation of life. Furthermore, as also discussed in chapter three, there are significant differences in the interactions of those on the biology side of synthetic biology, and those on the engineering side, with the discipline's 'products.'

The biologists, as outlined in chapter three, predominantly encounter their 'products' within the messy reality of the laboratory, where cultures die and thrive, need to be tended, fed, and kept alive. An environment where the organisms are as likely to throw up aberrant results requiring experiments to be tweaked or overhauled completely, as they are to produce the desired outcomes. These synthetic biologists also encounter their 'products' through inscriptions of various sorts, smeared lines on a black and white gel photo for example, or a series of OD[110] readings. But ultimately these, like the mathematical equations produced by modellers, do not supplant their impressions of the organisms themselves.

Many of the engineers, by contrast, only ever encounter these same 'products' in the form of numbers. First the cleaned, repeated, accurately timed results of experiments fed to them by the biologists, and then in the form of the mathematical equations that they turn these results into. As Callon's (1986) fascinating paper about scallop domestication showed, organisms are capable of different things when they are organisms than when they are reduced to being numbers. The numbers may be easier to work with, but they can mask the underlying complexity.[111] Thus it is perhaps easier for the engineers to adhere to a reductionist view of life and biology than it is for the biologists. Such a reductionist view is, after all, in line with the way other branches of engineering view their material and subjects. This does not however mean that it is necessarily an appropriate way of viewing and interacting with biology.

As shall be discussed in chapter six, famous microbiologist and biophysicist Carl Woese railed against the application of engineering's reductionism to biology. Although his comments predate the emergence of synthetic biology, he opposed both the idea of turning biology into an engineering discipline and the 'organism as machine' perspective, which underpin the discipline. He

[110] Optical Density.

[111] In Callon's study the numbers, which were meant to represent the scallops, displaced the scallops themselves but ultimately proved to be unrepresentative, leading to the drawing of inaccurate conclusions regarding the scallops' behaviour (1986).

wrote, "[l]et's stop looking at the organism purely as a molecular machine. The machine metaphor certainly provides insights, but these come at the price of overlooking much of what biology is" (2004: 176). Thus much like Canguilhem (2009) and Greco (2005), Woese argues that, "to understand living systems in any deep sense, we must come to see them not materialistically, as machines, but as (stable) complex, dynamic organization" (2004: 176).

Consequently, both Canguilhem and Woese might now have looked approvingly at the uncertainty and internal conflict of the synthetic biologists at the Centre. Seeing their ambiguous responses regarding the classification of their 'products' as a positive sign of resistance to the reductionism that is prevalent in modern biology. They might therefore, encourage the synthetic biologists at the Centre to embrace their doubts regarding the mechanistic conception of the organism, hold tight to their questions, and acknowledge their ignorance, rather than urge them to shed these in favour of the kind of certainty displayed by Michael. Arguing that such an approach is more likely to increase their understanding of the entities they work with than an unquestioning acceptance of the reductionism and mechanism that synthetic biology promotes.

Conclusion

The questions: 'what is life' and 'what are the essential differences, if any, between the living and the non-living/the animate and the inanimate/ organisms and machines?' have, as I address above, been with us since at least the fourth century BCE. Since this time, many attempts have been made to answer them. Yet, despite centuries of effort bringing us closer to an answer of what makes life, life, and to either firmly establishing or fully discrediting the existence of such boundaries, uncertainty remains. Enough uncertainty for vitalism to, as Canguilhem would have it, retain its vitality. Thus, despite the increasing certainty that life contains no metaphysical element, vitalism's persistent longevity suggests that Greco (2005), Bergson (1983), and Canguilhem (2009) are correct that the term highlights something important. As Greco (2005) argues, it appears to signpost a discomfort with mechanism and reductionism while affixing a label to our areas of ignorance regarding life, much as the more contemporary, and less contentious, 'complexity' now does. That is, while biological systems may well be explainable in terms of physico-chemical processes, there are too many unaccounted for differences between organisms and machines, and, as shown most recently by syn3.0 (Clyde A. Hutchison et al. 2016), too much that is unknown about life, to do away with the machine/organism divide completely; at least for now.

Given this degree of complexity, it is no great surprise that synthetic biology has struggled to implement its mechanistic approach. Nor is it alarming that those working with the messy reality of biology have struggled to conceive of these complex entities being completely reduced to simple physico-chemical components and processes. Where Venter displayed complete confidence that 'Synthia' required a new classificatory label, being not just life but synthetic life, the synthetic biologists at the Centre were largely more conflicted.

While most of the members of the Centre contended that no clear boundary exists between machines and organisms, most were more inclined to place the 'products' of their discipline in a blurry, grey, liminal zone between these categories, than to do away with the categories completely. Indeed, while several members of the Centre made claims regarding the homogeneity of all matter, animate and inanimate, only Michael stuck, unwavering, to this viewpoint. Most found themselves back-pedalling, or contradicting themselves as they tried to articulate what category the 'products' of synthetic biology belong within. This uncertainty and difficulty with attributing the 'products' to one category or the other may, I suggest, indicate the need for a new hybrid category. A boundary spanning conceptual category that is, which can encompass entities that possess characteristics of both machines and organisms simultaneously. Such a category would not only potentially solve synthetic biology's classification woes but more fundamentally, would disrupt the long held machine/organism divide.

The key word here however is conceptual given that, as I have discussed above, the process of classifying entities uncovers underlying philosophical conceptions about what counts as life, and what counts as a machine. Drawing on Keller I argue that both life and machine are human rather than natural categories, and the act of drawing a boundary, and assigning an entity to one or the other side, tells us something about the differences that are being honoured. The same would, of course, be true of such a hybrid boundary spanning category, should it arise. However, as it stands, those at the Centre honour a wide range of differences from which they have formed their concepts of what life and machines are. These honoured differences are then used as both justification of the classification given to their 'products' and as a guideline of what characteristics an entity would need to shed and/or gain in order to be deemed to have transgressed the machine/organism boundary; an achievement that for many is just a matter of time.

Yet, despite such goals, and despite claims that synthetic biology's 'products' fall within a grey zone, for which our existing categories are insufficient, the synthetic biologists at the Centre were hesitant to claim that synthetic biology is, as yet, producing anything revolutionary. For some, this was because life will always be life no matter what they do to it, but for others there seemed to be humility; a reluctance to court the media attention that a Venter-like announcement would garner, and the almost inevitable charges of playing God that come with 'creating' life. Yet, given the advances synthetic biology is making, and the work that the synthetic biologists at the Centre are engaged with, the reality is, as Deplazes and Huppenbauer argue, that the 'products' of their work "will affect the concept and evaluation of life and the idea of what constitutes a machine in society and in our culture" (2009: 63). Thus, while they may struggle with classifying their 'products,' and they may waiver back and forth between embracing mechanism and vitalism/complexity, given the nature of their work, they are likely to still face the same questions and concerns as Craig Venter did over 'Synthia.'

Chapter Six: Doing Biology Differently

As discussed in the previous chapter, synthetic biology is challenging our concepts and evaluations of organisms and machines. With its engineering approach to understanding and engaging with biology, this emerging discipline is promoting an extreme form of reductionism and mechanism. A mechanistic reductionism, that is, which ascribes to the notion that biology can be thought of and treated like any other engineerable material. Life, it is maintained, can be, or at least will be, designed, built, and controlled from the bottom up in the manner of machines. Performing predetermined, desired tasks, and producing industrialisable products. As discussed in chapter five, this approach is challenging the machine/organism boundary by arguably producing boundary spanning entities which, conceptually at least, bear characteristics from both sides. Thus, despite the practical and conceptual challenges synthetic biology is facing as it strives to establish itself as a discipline, I would maintain that this emerging discipline is, nevertheless, part of a larger, and more significant, shift within the life sciences. A movement, that is, towards convergence and collaboration between biology and engineering, which is reshaping our conception of life.

Scientific convergence

In 1939, Massachusetts Institute of Technology President, and physicist, Karl Compton and Professor of Biology John Bunker wrote a paper on the formation of biological engineering.[112] In it, they argued for open-mindedness,

[112] They describe their proposal of a five-year course of undergraduate and graduate work at MIT in biological engineering that they argue would be required to give students the necessary minimum training in the essential elements of biology, chemistry, and physics. This five-year course started in 1936 with students pursuing a BSc in Biophysics and subsequently an MSc in Biological Engineering. They write that much thought and consultation went into the choice of the name 'biological engineering' for the course. Apparently they temporarily abandoned it as a name while searching for an appropriate title for their objective however

and the importance of convergence between sciences, claiming that the history of science is like a pendulum swinging back and forth between periods of specialisation and periods of convergence. "Convergence of specialized fields," they argued, "comes about when some fundamental discovery discloses the underlying unity, the basic processes, of two branches of science which have developed apparently divergently on less fundamental and apparently unrelated bases" (1939: 7).

Compton and Bunker attribute many great intellectual and social advances to such convergences between disciplines. Arguing, in the case of their proposed 'biological engineers,' that they would be explorers of an "ill-mapped territory" (1939: 14) who may, like Christopher Columbus, come upon a new world serendipitously. Yet despite the name, Compton and Bunker included no engineers, nor engineering, in their endeavour. Rather, they envisioned their new field emerging at a time of convergence between biology, physics, and chemistry. However now, more than seventy years after their article proposing the field of biological engineering, engineering is itself entering the realm of biology. For just as biological engineering was framed by Compton and Bunker as the product of an underlying unity between biology, physics, and chemistry, the nascent field of synthetic biology is founded on a belief in an underlying unity between biology and engineering.

However, contrary to Compton and Bunker's assertions, I would argue that the current convergence between biology and engineering is more a result of assimilation that of an uncovered, fundamental unity between the disciplines.

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returned to it after rejecting 'biophysics' for being insufficiently definitive, 'biochemistry' for being insufficiently inclusive, and 'biurgy,' 'biodynamics,' and 'biotechnology' for being unsuitable. Dr Vannevar Bush, then the vice-president and dean of engineering at MIT (who, interestingly, later became one of the primary organisers of the Manhattan Project), encouraged the use of the name 'biological engineering,' even though those who decided to use it, didn't, at the time, like it. Bush argued that their objective conformed to the definition of engineering as "the art of organizing and directing men and of controlling forces and materials of nature for the benefit of the human race" (2009b: 294) Within this conception of engineering the authors argue there was scope for "every activity from instrumentation to theory, including biophysics and biochemistry . . . so long as the major objective is the marshalling of all available resources to aid biology for the benefit of humanity" (Compton and Bunker 1939: 12).

A general movement, that is, of both disciplines towards a point of convergence. As biology slowly but surely is reformulated in the image of engineering, and engineering encroaches further and further into the life sciences. Where this expansion of engineering was discussed in chapter three, it is the shifts in biology that I believe are more significant to the development of synthetic biology. As such it is biology that I shall focus on in this chapter.

In *A Vital Rationalist*, Georges Canguilhem (2000) writes of four major shifts in the conception of life; life as animation, life as mechanism, life as organisation, and life as information. These shifts take us from Aristotle, in 350BCE, right up until the end of the twentieth century. As I shall address, they have come about as the result of scientific and technological advances and societal and philosophical shifts as we have continued our attempts to grapple with the stuff of life. All have been focused on understanding life and its processes, but all, as I shall address, have also introduced concepts and practices that have incrementally moved biology closer to this intersection with engineering. Indeed, as mechanism has encroached further and further into our understandings of life we have moved closer and closer to a convergence between biology and engineering. To the so-called crossroads between biology and engineering where synthetic biology is said to reside (Rusk 2007).

Echoing a British Medical Journal (BMJ) article from 1910 (BMJ 1910), Compton and Bunker (1939) wrote that, the introduction of experimental techniques from physics and chemistry into biology changed the character of biology from descriptive to analytical. Yet where Compton and Bunker leave their analysis at this point, the BMJ paper asserts that "[a]ll natural science follow the same process of evolution" (1910: 1080) beginning with a descriptive phase, followed by an analytical phase, and advancing to a synthetic phase. "Biology," the author lamented over a hundred years ago, had "not yet advanced beyond the first two stages" (BMJ 1910: 1080). Yet, it seems that it is just such an 'advance' that synthetic biology is now attempting to enact, both in name and in practice, as they shift the focus of their biology from analysis to synthesis. A shift which is clearly articulated by Venter's team when, regarding the creation of syn3.0's minimal genome, they write:

> "Genomics is moving from a descriptive phase, in which genomes are sequenced and analysed, to a synthetic phase, in which whole genomes can be built by chemical synthesis. As the detailed genetic requirements for life are discovered, it will become possible to design whole genomes from first principles, build them by chemical synthesis, and then bring them to life by installation into a receptive cellular environment" (Clyde A. Hutchison et al. 2016: 8).

In this chapter then, I shall take a step back from the Centre and the day-to-day work which takes place within it, in order to investigate both the shifts in the character of biology, and in the conception of life, which are captured in the above quote. This is not intended as a 'glossing over' of the challenges of enacting synthetic biology's engineering approach, but rather as an acknowledgement that, in spite of these challenges, the landscape of biology appears to be shifting. Thus drawing from scientific, philosophical, historical, and social science literature, I shall explore the wider social and scientific trends that have ultimately led to this point of convergence between biology and engineering. A junction where, the momentum towards engineering, the growing technologisation of life, and an increasingly interventionist approach to biology, are culminating in an emerging shift in the conception of life.

The beginnings of biology

The origins of the word 'biology,' as the name for a distinct science of life, are often traced back to a varying number of independent scientists working at the turn of the nineteenth century.[113] Yet the roots of the word, like the

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[113] Most commonly the coinage is attributed to German naturalist and botanist Gottfried Reinhold Treviranus and French botanist and natural historian Jean-Baptiste Lamarck (Canguilhem 2000; Keller 2002; Sapp 2003). However it is sometimes also attributed to German physiologist and medical historian Theodor Georg August Roose (Mateos 2010), French anatomist and physiologist Marie François Xavier Bichat (Gayon 2010), and German physiologist Karl Friedrich Burdach, (Mayr 1982). These independent coinages all took place between 1797-1802 (Compton and Bunker 1939).

roots of the discipline, go back much further. Biology, in its Latin form '*biologia*,' is the contraction of the Greek word *bios*, meaning 'life,' and the suffix *–logia*, meaning 'study of.' Gayon writes that, in this form, the word has been used since at least the seventeenth century in German speaking universities. However, it's purpose was solely descriptive, being used primarily in obituaries to denote the narrative of an individual's entire life (2010).[114] As such, Richards claims that it wasn't until 1802 that Treviranus established the modern concept of biology,[115] describing the science as follows:

> "The objects of our research will be the different forms and manifestations of life, the conditions and laws under which these phenomena occur, and the causes through which they have been effected. The science that concerns itself with these objects we will indicate by the name biology [Biologie] or the doctrine of life [Lebenslehre]" (Treviranus quoted in: Richards 2002).[116]

While modern biology remains closely linked to this conception of the science, Sarah Franklin (1995) argues that our understanding of life has transformed many times in the intervening years. While I would agree with Franklin, I would, following Canguilhem (2000), extend her assertion to the

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[114] According to McLaughlin (2002), the word reappeared in 1736 when Swedish natural scientist Carl Linnaeus, used the term *biologi* in his *Bibliotheca botanica.* However its usage, at this time, was similarly descriptive and denoted what we might now call biography.

[115] McLaughlin attributes to German professor and librarian Michael Christoph Hanov, the word's usage as a referent to a general science of life, one that embraces both plants and animals. This was in the third of his four-volume Latin compendium, a volume bearing the wonderfully loquacious subtitle: *Geology, Biology, General Phytology and Dendrology, or the Science of the Earth, of Living Things and of Vegetating Things in General, as well as of Trees* (*Philosophiae naturalis sive physicae dogmaticae tomus III, continens geologiam, biologiam, phytologiam generalem et dendrologiam vel terrae, rerum viventium et vegetantium in genere, atque arborum scientiam).* The compendium itself was entitled *Natural Philosophy or Dogmatic Physics* (*Philosophia naturalis sive physica dogmatica*) and was originally published between 1762-1768. However, rather than envisioning it as a broad discipline encompassing all of botany and zoology, Hanov reportedly used 'biology' to refer solely to the study of 'laws' common to both plants and animals (Gayon 2010; Mateos 2010; McLaughlin 2002). Moreover, with the exception of headings, Hanov does not use 'biology' in his work at all and thus his use of the term, according to McLaughlin (2002), probably did not influence later coinages.

[116] It was, however, only in the years following 1840, once French philosopher Auguste Comte popularised the word, that 'biology' came into common use (Gayon 2010).

period of time before 'biology' was coined. For as Canguilhem writes, our understandings of 'life' have varied widely since it was first defined 2366 years ago. Nevertheless, one must be careful when looking at earlier understandings of what we now consider 'life,' that these are not attributed to the science of biology per se. Foucault was quick to warn historians against such 'histories' of pre-nineteenth century biology, writing:

> "they do not realize that biology did not exist then, and that the pattern of knowledge that has been familiar to us for a hundred and fifty years is not valid for a previous period. And that, if biology was unknown, there was a very simple reason for it: that life itself did not exist. All that existed was living beings, which were viewed through a grid of knowledge constituted by *natural history*" (1970: 127-28).

Natural history, which predated biology, was indeed concerned with living beings rather than the phenomenon of 'life.' However there were, as I shall discuss below, attempts to define what it was that distinguished animate entities. While such attempts may not have employed the term 'life,' I would argue that we would now, in hindsight, consider these attempts to be attempts to define life. As such, and for the benefit of continuity, I shall speak of life before Foucault would perhaps consider it appropriate. As mentioned previously, Canguilhem (2000) divides the history of the conception of life into four main periods, namely, life as animation, life as mechanism, life as organisation, and life as information. Below I shall briefly explore each of these ways of conceptualising life in order to argue that the study of life has been incrementally shifting towards the notion of life as engineerable material since its inception.

Life as animation

Canguilhem quotes Aristotle as writing, in his 350BCE treatise *De Anima*, "[o]f natural bodies [that is, those not fabricated by man], some possess vitality, others do not. We mean by 'possessing vitality' that a thing can nourish itself and grow and decay" (Aristotle quoted in Canguilhem 2000: 67). This, Hanov (1997) claims, was the first known attempt to provide a general definition of life.[117] For two centuries before Aristotle, his predecessors had written down their reflections on nature, seeking to discover the simplest entities in the universe in order to provide a bottom-up understanding of nature (Lennox 2001). But until Aristotle, no one had singled out living natural entities as a group worthy of a distinct branch of natural philosophy. Indeed, in contrast to his predecessors, Aristotle reportedly preferred to focus on the perceived unity of form and matter within all animate entities, arguing that it was life that distinguished the animate from the inanimate (Canguilhem 2000). Aristotle's notion of life as animation thus became the first known conception of life (Canguilhem 2000). Under this conception, Gayon notes, life was intimately associated with the concept of the soul. Wherein the soul is understood as being "for the entire body what sight is for the eye . . . both the ensemble of functions, and their coordination" (Gayon 2010: 236).[118]

Yet despite his adherence to what some claim is a vitalistic conception of the organism (R. E. Hughes 1965), Aristotle also introduced mechanical evaluations and comparisons into his assessment of animate entities. As Canguilhem notes, Aristotle held that a slave was, essentially, "an animate machine" (2009: 80). Canguilhem (2009) also notes that Aristotle, like Plato before him, likened the movement of limbs to mechanisms. Thus, despite the long held conceptual division between machines and organisms, discussed in chapter five, Aristotle's work not only served as the beginning of the study of life but also the beginning of the encroachment of mechanism into biology. While also serving as the first "assimilation of the organism to a machine"

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[117] Given that, "except for some medical lore, we have next to no information about the biological knowledge of the Sumerians, Babylonians, Egyptians, and other civilizations preceding that of the Greeks" (Hanov 1997).

[118] Aristotle is also widely quoted as arguing that, in animate entities, "the whole is something over and above its parts and not just the sum of them all" (Corning 2002: 19). Thus, Ruse (2013) contends that Aristotle's focus was on questions of purpose and ends, arguing that in order to gain full understanding of an animate entity one needed to ask about final causes, to trace how their potentiality translated into their actuality.

(Canguilhem 2009: 79).[119] These, it would seem in hindsight, were the first steps along the road towards biology's current convergence with engineering. However, due to both the increasing role of Christianity in the West, and the domination of essentialism in Western thinking, it was several centuries before any further steps were taken along this path.[120]

The Renaissance and the scientific revolution

After many centuries of little progress in the natural sciences, the Renaissance saw a renewed interest in natural history and anatomy. Explorers and traders had started travelling further around the globe bringing back tales, and indeed evidence, of the sheer diversity of the planet's plant and animal life (Mayr 1982). Faced with this abundance of life, Foucault (1970) reports that

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[119] In *Knowledge of Life*, Canguilhem explores the history of the assimilation of organisms as machines, which underlies the assumptions of Descartes, and his followers, regarding animals. Long before Descartes, Aristotle argued that animals were machines, comparing their movements with those of war machines (for example he likened the movement of the arm to that of the catapult). In this way, Canguilhem asserts, Aristotle was faithful to Plato who similarly defined the movements of vertebrates on the basis of pivots. This assimilation of organisms as machines thus predated Descartes and fed through Descartes' ideas, and ultimately into his mechanical philosophy and mechanistic approach to biology (P. R. L. Brown 1971).

[120] Mayr (1982) contends that for more than two thousand years following the work of Aristotle and Plato, Western thinking was dominated by essentialism. A concept maintaining that any specific entity has a set of innate, and thus unchanging, characteristics and attributes which make them what they are and which can therefore be used to identify them. This perspective was, reportedly, adopted by Christian theology. However the Greek notion of an eternal, essentially static world was not. Instead Christian theology, Mayr writes, was dominated by the concept of creation which held that the world is not eternal, but rather recently created, and all knowledge of the world is contained within the Bible's "revealed word" (Mayr 1982: 91). This perspective both precluded the need to ask 'why' questions and, by asserting that all nature (plants and animals) was subservient to humans, disrupted the Greek idea of a unity in nature. Furthermore, Mayr notes, this so-called natural theology adhered strictly to rationalism, maintaining that truth could be deduced through logic and reasoning rather than observation or experiment. Indeed empiricism, promoted by Aristotle and now the backbone of modern science, was despised. The dominance of natural theology, which looked to nature solely to provide arguments for the existence of God, was thus thoroughly unfavourable to the development of the natural sciences (Mayr 1982). Indeed throughout the Middle Ages, (considered to have lasted in Europe from the 5th to 15th century) "[t]he only aspects of living nature that received attention were problems of medicine and human biology" (Mayr 1982: 93) and even here empirical investigation played only a minor part. For example, while anatomy was taught in Medieval medical schools, dissection played only a small part in the teaching. Thus it wasn't until the Renaissance (considered to have lasted from the fourteenth until the seventeenth centuries) that the study of life began to progress beyond the work of Aristotle.

many natural historians turned to Aristotle's approach to studying life, classifying everything into taxonomies based on their observable, and only their observable, characteristics.[121] Thus, just as it had been under Aristotle, the study of life at this time was very descriptive in character. Yet despite its descriptive nature, such taxonomic work played a significant role in reigniting the scientific study of life.[122]

Following this reintroduction of scientific practice, further steps were taken to move away from the constraints of natural theology. For example, Smith (2011) writes that in the early seventeenth century 'psychology,' understood at the time to be the analysis of the soul, was eliminated from the study of the natural world. As a result of this elimination, some saw a need to replace the soul, previously considered to be responsible for the animation of nature, with something else. Smith argues that this replacement "took the form of the concept of 'life,' but the challenge for many seventeenth-century thinkers was to find a way to study life, or to 'do biology,' without allowing this to be simply a continuation of psychology under a new name" (2011: 3). At this same time, the scientific revolution was growing, and with it, Ruse notes, came "a fundamental change in the root metaphor that informs everything" (2013: 412). The new "root metaphor," ushered in by the Scientific Revolution, was mechanism. The focus thus shifted from life as animation's organic view of the world, where everything was looked at in terms of living beings, to a mechanistic worldview where everything was looked at in terms of machines.

[121] Mayr writes, "[t]he era of overseas travel and explorations resulted in a veritable obsession with exotic organisms and led to the establishment of vast collections" (1982: 101) The exponential growth of such collections produced a drive towards classification starting with Cesalpino (1583) and reaching a climax with Carl Linnaeus (1707-1778). Thus, even eighteenth century naturalists, such as Comte Buffon and Linneaus, drew heavily on Aristotle in their work, describing and classifying life forms without ever defining what they meant by 'alive.'

[122] Another significant factor in this reintroduction of scientific practice into biology was the role played by dissection in the teaching of anatomy. Dutch professor of medicine Andreas Vesalius made dissection a central, rather than a supplementary, element of his practice and teaching thus helping to bring observation and empiricism back into the study of life (Vesalius et al. 1973).

Thus, Ruse (2013) writes, the focus shifted from animism and final causes, to laws of motion and 'blind' physical forces.

In introducing this new mechanistic worldview the study of life moved closer to a point of convergence with engineering, laying the initial mechanistic groundwork for the conceptual shift towards engineering that we are currently seeing in the life sciences. People at this time began to think of nature as "a law-bound system of matter in motion" (Mayr 1982: 95) believing that all motion, whether organic or mechanical, had to have a mechanical cause. Thus it was that by 1600, 950 years after it was first advanced, "the concept of life as an animation of matter lost ground to materialist or merely mechanistic conceptions of the intrinsic life functions" (Canguilhem 2000: 75).

Life as mechanism

As Osler (2004) writes, the development of mechanistic philosophy was a collective endeavour undertaken by a community of European thinkers during the first half of the seventeenth century.[123] Yet, no other member of this community, Nicholson (2012) argues, contributed more to the spread of the mechanistic worldview into the natural sciences than French philosopher René Descartes. Adamant that animals were essentially machines, Descartes famously proposed a vision of life that reduced all organisms to a class of automata. Writing in regards to animals, "I should like you to consider that these functions follow from the mere arrangement of the machine's organs every bit as naturally as the movements of a clock or other automaton follow from the arrangement of its counter-weights and wheels" (1988: 108). Thus Canguilhem writes that, in perceiving animals as machines, "Descartes does to the animal what Aristotle did to the slave: he devalorizes it in order to justify its use by man as an instrument" (2009: 84).[124]

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[123] Osler (2004) writes that the core members of this community were Isaac Beeckman, Marin Mersenne, Thomas Hobbes, Pierre Gassendi, René Descartes, Sir Kenelm Digby, and Walter Charleton.

[124] Despite his focus on animals, human beings were not exempt from Descartes' mechanism, they were however considered to be significantly different to all other organisms. For, while animals were deemed to be merely machines, humans, Descartes contended, possessed

By envisioning life as mechanism, and thus all living entities as instruments and machines, Descartes took a position in direct opposition to that of life as animation. Where life as animation suggested that living beings were distinct from non-living entities, and therefore required a special type of explanation, life as mechanism held that there were no such distinctions and thus no need for a special theoretical principle to explain their functioning. Indeed, Descartes reportedly challenged the machine/organism divide, much as modern synthetic biology does (as discussed in chapter five), by contending that organisms are not merely analogous to machines but that ontologically they can be identified as machines (Nicholson 2013).

Thus, despite external similarities with the mechanistic theory of movement advanced by Aristotle, Canguilhem (2009) contends that the theories of movement of Aristotle and Descartes were in fact very different. Where Aristotle held that, despite the mechanistic nature of movement, "the principle of all movement is the soul," and that all movement requires a "first motor" (Canguilhem 2009: 79), Descartes' theory of movement was not reliant on the soul at all. Rather, Descartes attributed all organic movement to the same mechanistic origins as he determined were responsible for machine movement.[125] The whole for the organism, as for the machine, being seen as "strictly the sum of the parts" (Canguilhem 2009: 88). Thus under Descartes' life as mechanism, the explanations for the movements and functions of mechanical machines were, Gayon (2010) notes, applied without alteration to

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rational, nonmaterial souls, or minds, which interacted with the material and mechanical body through the pineal gland. It was this distinction of mind and body that became the basis of Cartesian dualism (Descartes 1988).

[125] Canguilhem argues that in both cases the source of the energy fuelling the movement is either human or animal, however this is often ignored under Descartes' theory of movement due to the time between the storing and releasing of the 'organic' energy. Canguilhem writes: "[d]espite this difference in the explanation of motion, the fact remains that for Aristotle, as later for Descartes, the comparison of the organism to a machine presupposes man-made devices in which an automatic mechanism is linked to a source of energy whose motor effects continue well after the human or animal effort they release has ceased. It is this interval between the storing up and the release of energy by the mechanism that allows one to forget the relationship of dependence between the mechanism's effects and the action of a living being" (2009: 79-80).

organisms. In this way, Descartes moved the study of life closer to engineering, while also expanding mechanistic understandings of life to encompass the parts, the whole, and the function of all organisms.

Such a belief in the homogeneity of machines and organisms is, according to Nicholson (2013), based on a number of readily perceptible commonalities. For example, both are bounded physical systems whose actions are governed by natural laws. Both use energy and are hierarchically structured and differentiated internally, and both can be described in terms of causal relationships between interacting parts. Ultimately then, both are organised so that, as a whole, they are purposive, working towards the attainment of particular ends (Nicholson 2013).[126] Yet despite such commonalities, there was another motivation for reframing biology using the concept of mechanism. As Mayr writes, "[o]ne of the objectives of attempts to provide a mechanistic explanation of all phenomena was to further the unity of science" (1982: 99).[127]

Central to this drive for unity was, reportedly, the work of Newton. For example Clayton writes, "nothing seemed more to support a mechanistic worldview than Isaac Newton's three laws" (2013: 435). Published in 1687, Clayton argues that "[t]he brilliance of Newton's laws was that they proposed a single quantitative dynamical system that could in principle account for the motion of all physical bodies whatsoever. It was this assumption, among others, that made possible the birth of the scientific method" (2013: 435). It was also an assumption which, Mayr (1982) contends, greatly reinforced the mechanistic approach to physiology.

In attempting to align the natural sciences with the physical sciences, as the scientific method came into being, Compton and Bunker (1939) assert that the

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[126] However, as both Nicholson (2013) and Canguilhem (2009) note, the nature of their purposiveness is completely different.

[127] During the Renaissance all areas of science saw great advancements, and with these advances came a desire to bring the natural sciences in line with the physical sciences. Indeed Mayr (1982) writes that, during the seventeenth century, natural scientists looked increasingly to the notion of life as mechanism to describe and understand the world. This drive under mechanism to cast biology in the image of physics is, Clayton (2013) notes, an interesting reversal of the desire, under life as animation, to cast physics in the image of biology (Shapin 1996).

study of life began to shift in character from being descriptive to being analytical. This shift is evident in Mayr's (1982) descriptions of seventeenth and eighteenth century iatromechanics.[128] A movement which attempted to explain the workings of organs or organ systems by building 'mechanical models' and drawing on the laws of Galilean and Cartesian mechanics (Mayr 1982). Thus leading Mayr to write, regarding this time, "[m]ore than ever, it now became fashionable to explain everything in physical terms of forces and motion, as inappropriate as such an explanation was for most biological phenomena" (1982: 96).[129] Consequently Mayr (1982) notes that, despite its success, Descartes' notion of life as mechanism encountered vigorous resistance from some biologists, mainly in the form of anti-reductionistic, anti-mechanistic, vitalistic arguments.

Vitalistic objections

While in today's world, contending that organisms are not essentially the same as machines, but rather are fundamentally and essentially different, is to court the pejorative charge of vitalism, vitalism did not always garner such scientific scorn. Indeed in the seventeenth and eighteenth centuries, Descartes' mechanistic approach to biology was unpopular among naturalists, who contended that there was much about animate entities that defied mechanistic explanation.[130] Questions such as, "how can a machine regenerate

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[128] Iatromechanism was an intellectual movement that advocated the study of the mechanics of living beings (Canguilhem 2009).

[129] Canguilhem likewise contends that such explanations of life are inappropriate. Arguing that, "mechanism is a theory that tells us how machines (living or not) work once they are built, but it tells us nothing about how to build them" (2000: 78).

[130] More recently Nicholson and Canguilhem have written extensively on the differences between machines and organisms. Organisms, they contend, act on their own behalf, working towards their own ends, while machines do not serve their own interests, only those of their maker or operator. Indeed, both authors assert that machines, unlike organisms, are not autonomous. Where organisms demonstrate "self-construction, self-conservation, self-regulation, and self-repair," in order for machines to display these processes, Canguilhem notes, they require the "periodic intervention of human action" (2009: 88). Canguilhem also argues that in machines, "the whole is strictly the sum of the parts," while machines themselves display a clear functional rigidity "made increasingly pronounced by the practice of standardization" (2009: 88). An organism, by contrast, is described as having "greater latitude of action than a machine. It has," Canguilhem asserts, "less purpose and more

lost parts, as many kinds of organisms are able to do? How can a machine replicate itself? How can two machines fuse into a single one like the fusion of two gametes when producing a zygote?" (Mayr 2002) went unanswered under Descartes' mechanism.[131] Thus, as a result, vitalists argued that animate entities must "contain some non-physical element or [be] governed by different principles than are inanimate things" (Bechtel and Richardson 1998) and thus they cannot simply be reduced to physico-chemical components and equated with machines. Vitalists concluded that, "just as the motion of planets, suns, and stars, is controlled by an occult, invisible force called by Newton gravitation, analogously the movements and other manifestations of life in organisms is controlled by an invisible force, Lebenskraft or *vis vitalis"* (Mayr 2002).

Other scientists were, however, so convinced by the essential truth of life as mechanism that they took to their laboratories to attempt to prove the fundamental homogeneity of organisms and machines. Endeavours to this ends have included various attempts to reduce life phenomena to replicable physical-chemical processes, as French scientists Lavoisier and Laplace did in 1780 in regards to the formation of animal heat (Loeb 1912)[132] and Wöhler did in 1828 with the synthesis of urea.[133] The success of such experiments helped to

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potentialities" (2009: 90). A further significant difference between organisms and machines is said to be death. Death, Canguilhem writes, "is what distinguishes living individuals in the world, and the inevitability of death points up the apparent exception to the laws of thermodynamics which living things constitute. Thus the search for signs of death is fundamentally a search for an irrefutable sign of life" (2000: 88). Consequently, Canguilhem is arguing that in deteriorating and dying in the manner that they do, organisms further highlight their differences from machines, which, while they also cease to function, do not die.

[131] However it should be noted that modern biology, through advances in genetics and molecular biology, has solved these questions without the need for a vital force.

[132] Their experiment demonstrated that the quantity of heat formed in the body of a warm-blooded animal was equal to that formed in a candle, provided that the same quantity of carbon dioxide was formed in both cases.

[133] This experiment is often credited, somewhat inaccurately, with single-handedly refuting vitalism. The argument goes that by synthesising this organic compound out of two inorganic molecules, Wöhler challenged the vitalistic belief that, organic compounds could only be formed from other organic compounds and therefore a fundamental difference existed between them and their inorganic counterparts (Bruce Fye 1996).

cement the notion of life as mechanism, and the belief in the homogeneity of machines and organisms, while simultaneously eroding the credibility of vitalism. Consequently, despite the continued resistance of vitalists,[134] the notion of life as mechanism, as evident in the advent of synthetic biology, has not disappeared. What has changed across the centuries however are the analogies drawn upon, as organisms have come to be understood in terms of the paradigmatic machine of the age (Nicholson 2013). Nicholson writes that in the seventeenth century it was the clock, in the eighteenth century, the steam engine, in the nineteenth century, the chemical factory, and in the twentieth century, the computer (Nicholson 2013). Yet, despite the enduring perseverance of mechanistic analogies, and mechanistic conceptions within biology, Canguilhem (2000) argues that, like the notion of life as animation before it, Descartes' conception of life as mechanism did eventually fall out of favour. Spurred along, in part, by the rise of microscopy.

[134] For example, in both *Knowledge of Life* (2009) and *A Vital Rationalist: Selected Writings from Georges Canguilhem* (2000), Canguilhem questions both the conflation of organisms and machines, and the use of machines as a model to understand organisms. He contends that, with the exception of vertebrates, organisms rarely behave in ways that would evoke the idea of a mechanism. Furthermore, he argues that both Descartes' and Aristotle's comparisons of organisms and machines "presupposes man-made devices in which an automatic mechanism is linked to a source of energy whose motor effects continue well after the human or animal effort they release has ceased" (2009: 79-80). However, he continues, "this explanation can only be conceived once human ingenuity has constructed apparatuses that imitate organic movements" (2009: 80). What Canguilhem is therefore arguing is that machines can only be used to explain organisms once organisms have designed and built them to imitate organic movement. As he puts it, "the construction of a mechanical model presupposes a vital original" (2009: 85). This is significant because, as Nicholson (2013) notes, the tendency to metaphorically describe organisms as a class of machine, as was undertaken under the conception of life as mechanism, is based on the assumption that, in doing so we are able to come to terms with many of the organism's properties and features. However Canguilhem contends that since organisms precede machines, to explain any similarities found within organs or organisms through mechanical models is "to explain the organ using the organ. It is a tautology" (2009: 87).

The rise of microscopy

First invented in the 1590s (Van Helden et al. 2010), microscopes came into common usage for research in the second half of the seventeenth century (Wootton 2006). Mechanism, Canguilhem (2000) writes, had by this time become the dominant explanatory model for the structure and workings of organs such as the heart, muscles, and lungs. However, it was of little use in explaining the hidden inner structures of plants and animals revealed under the microscope (Canguilhem 2000). Seventeenth century mechanism was, after all, a theory based on data accessible to sight and touch. While "microscopic anatomy was concerned with objects beyond the manifest and tangible" (Canguilhem 2000: 79) and thus hinted at unimagined levels of structural complexity. On the basis of this limitation, Canguilhem (2000) notes that French mathematician, physicist, and philosopher Blaise Pascal, and German philosopher Gottfried Wilhelm Leibniz, found Descarte's notion of life as mechanism wanting. Leibniz's critique was, Canguilhem asserts, particularly significant as it lay the foundations for a new conception of living things, life as organisation (Canguilhem 2000; Leibniz 1930).

Life as organisation

Despite the continued popularity of the concept of life as mechanism, Gayon (2010) argues that life as organisation began to gain ground in the eighteenth century.[135] While still relying on mechanistic conceptions of the body, it also drew on Aristotle's notion of the 'organised body.' A notion which Canguilhem (2000) argues denotes the idea that animals (and to a lesser extent plants) are made up of instruments or organs, which are indispensible to the exercise of the organiser's, that is the soul's, powers. Yet, Canguilhem maintains that the naturalists, physicians, and philosophers who saw the benefit in such a combination of conceptions nevertheless sought semantic substitutes for the word 'soul.' In order "to explain how systems composed of

[135] Descartes also adhered to the notion of the organised body, however he saw no need for an 'organiser,' whereas Leibniz argued that without an organiser, nothing is organised (Canguilhem 2000).

distinct components nevertheless work in a unified manner to perform a function" (2000: 81). In the eighteenth century the concept of the 'organism' was, Gayon (2010) maintains, eventually settled upon as an alternative to 'soul.' Indicating, by definition, that an 'organism' was able to perform such feats of organisation.

Gayon (2010) writes that the term 'organism,' so familiar to us now, only entered common usage in the nineteenth century. This was largely as a result of Immanuel Kant's 1790 publication *Critique of Judgment* (Kant 1987). According to Canguilhem (2000) and Gayon (2010), Kant's work provided a clear, philosophical elaboration of the concept of life as organisation.[136] He argued that an organised body was a machine in one sense, but a machine that required a formative energy that was capable of organising otherwise inert matter, a feat beyond the powers of manufactured machines. Thus, Canguilhem writes, Kant conceived of the organic body as "not only organized, it is self-organizing"[137] (2000: 82) each part being an organ that produced the other parts. It was this notion that the whole is greater than the sum of its parts, and the focus on the intricate organisation of an organism, which Canguilhem (2000) claims set life as organisation apart from life as mechanism.[138] Kay quotes François Jacob's explanation of the notion of life as organisation as follows.

> "It was the interaction of the parts that gave meaning to the whole . . . The surface properties of a living being were controlled by the inside, what is visible by what is hidden. Form, attributes and behaviour all became expressions of organization. By its

[136] However he did so without using the words 'life' or 'living thing.'

[137] Able to self-maintain, self-repair, and self-reproduce (Gayon 2010).

[138] At the beginning of the nineteenth century, the concept of life as organisation gained further theoretical support from French philosopher Auguste Comte, who wrote that "the idea of life is really inseparable from that of organization" (Comte quoted in Canguilhem 2000: 83). Interestingly, and as noted previously, Comte was also responsible for the popularisation of the term 'biology.'

organization the living could be distinguished from the non-living" (Jacob quoted in Kay 2000: 40)

This shift in focus, Kay (2000) writes, was not only instrumental in the shift away from Descartes' notion of life as mechanism, and a reassertion of the machine/organism divide, but also facilitated the birth of 'biology' as a science. However, despite this shift, technological imagery and mechanistic conceptions persisted, as Canguilhem (2000) contends they had since the time of Aristotle. However, this mechanism now took a different form. The organism came to be seen as a "sort of workshop or factory" (Canguilhem 2000: 84), an "organic machine" equipped with a "flexible, elastic mechanism" which nevertheless does not violate the "general laws of mechanics, physics or chemistry" (Claude Bernard quoted in Canguilhem 2000: 86).[139] Thus, this new science moved away from classifying organisms on the basis of visible structures, and instead focused on studying organisation and the processes of life.

However, given its retention of mechanistic language and imagery this shift merely changed the mechanistic analogy for life. Organisms, that is, shifted from being viewed as machines to being viewed as factories. As such, despite bearing a different understanding of life than that of life as mechanism, life as organisation retained, and indeed expanded, the mechanistic conception of biology. A major component in this movement being the perspective that

[139] This notion of a flexible, elastic mechanism was also central to French naturalist Jean-Baptiste Lamarck's version of evolutionism, which he articulated in *Discours* (1800). In stark contrast to Descartes' mechanism, which held that species were fixed, Lamarck's research led him to believe that organisms were adapted to their environment. Mayr quotes him as writing, "they must change in order to maintain their adaptation to the ever changing world" (Mayr 1982: 108). While his explanatory endeavours encountered strong resistance within the naturalist community, and were largely unsuccessful due in large part to their reliance on conventional beliefs such as the notion that acquired characteristics were inheritable, Lamarck's work undoubtedly paved the way for Charles Darwin, whose *On the Origin of Species* (published in 1859) posited several revolutionary ideas (Mayr 1982). Firstly, he suggested that all life forms, humans included, shared a common ancestor, thus demoting them from the lofty position given to them by Christian dogma and Descartes. Secondly, he posited the theory of evolutionary causation, and the mechanism of natural selection which, Henning and Scarfe (2013) contend was responsible for mechanism conquering in the biological sciences, no less than it conquered in the physical sciences.

organisms are factories, a notion clearly still evident in modern day synthetic biology. This perspective thus spurred on the development of the increasingly interventionist approach to biology apparent today. For, in viewing organisms as sites of production, the focus of biology moved closer to that of engineering. A move, that is, which ultimately saw the beginnings of attempts to shift biology into a synthetic phase.

An interventionist approach to biology

The advent of leavened bread making and brewing, some 8000 and 4500 years ago respectively, arguably first demonstrated an interventionist approach to living organisms (Ladisch 2004).[140] However Bud contends that tracing modern interventionist biology back this far is misleading, given that "Egyptian craftsmen thought of their work in a way quite different from the modern technologist" (1993: 2). As such, I will begin my exploration of the interventionist approach to biology in the late nineteenth century with the work of Moritz Traube.

Moritz Traube is credited, by the BMJ (1910), with the construction of the first artificial cell, in 1864.[141] Yet the BMJ article claims that Traube's work, and that of several of his contemporaries who also strove to create 'life,' was largely ignored. Nevertheless, the article's author was certain that, as of the beginning of the twentieth century, things were about to change. To this ends, s/he[142] wrote:

> "The idea of biological synthesis is a bold one, and yet it is no novelty. It has cropped up in the imaginative literature of all ages, but, considered as a scientific possibility, its conception is of very recent date (BMJ 1910: 1080).

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[140] Both being processes which manipulate microorganisms in order to produce a product.

[141] Traube's artificial cell was formed using osmosis.

[142] The identity of the author is not supplied with the BMJ article.

To evidence the scientific possibility of biological synthesis, the article references the work of French biologist Stephane Leduc.[143] Being a firm believer in the virtues of synthesis, and not just analysis, in the advancement of biology, Leduc was, Campos writes, one of the first people to "experimentally attempt to use synthesis as a means to understand the basic biology of organic growth and morphology" (2009: 7). His experiments involved the use of osmosis and diffusion through which he created artificial 'cellular' systems that mimicked biological processes, and which Leduc (1911) claimed showed the physico-chemical foundations of life. It was this approach that he termed 'synthetic biology,' being the first, as far as I am aware, to coin this term.[144]

While Leduc's osmotic growths were inorganic, like living organisms they exhibited reproduction, assimilation, elimination, and morphogenesis.[145] It would therefore appear that such work was underpinned by a mechanistic conception of life that extended to the cellular level. A mechanistic conception, that is, which went deeper into our understanding of life and biology. One, that is, which held that replicating the physical structures of a 'natural' cell in a mechanistic fashion, could produce life. As the author of the BMJ article attests, it was believed that the form and function of cells, and therefore life, was achieved through osmosis. Thus by utilising osmosis to mimic the structures and transformations of the cell, one was essentially creating life.

> "[a]n animal or plant can live and grow by virtue of osmosis. Not only is osmosis responsible for the maintenance and continuance of life, however, but it is also capable of creating living matter from its

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[143] As well as Quincke of Heidelberg, Benedikt of Vienna, Dubois of Lyon, and Lehmann of Karlsruhe (BMJ 1910).

[144] This work and approach are described by Leduc (1911, 1912).

[145] Leduc was not alone in using inorganic compounds to explore the origins and structure of life. Irish physicist John Butler Burke, for example, grew 'life-like' cellular forms after introducing radium into sterilised test tubes of bouillon. While Burke did not claim that his structures were living, he believed that they weren't wholly inorganic either, seeing them instead as half-living (Burke 1906).

elementary constituents; it is, in fact, practically equivalent to the vital force we term life" (BMJ 1910: 1080-81).

Nonetheless, despite the enthusiasm of this author, and the resemblance of these osmotic structures to biological organisms, Keller notes that they raised questions in Leduc's contemporaries. Questions such as, "whether or not the resemblance was meaningful," and whether it provided answers "to questions about the nature and origin of real life" (2002: 47).

Although the idea underlying the work of Leduc, that living entities could be produced from inorganic matter, was far from a new one at the beginning of the twentieth century, Campos argues that this was a time when "a distinctively synthetic engineering-oriented standpoint to life gained dominance" (2009: 6). To illustrate this point, Campos describes the founding of the Carnegie Institution's Station for Experimental Evolution in 1904. The station's explicitly interventionist aim was to experiment with evolution so as to understand it, control it and direct it to the use of humanity.

This standpoint is clear in the following statements from Charles Davenport, the station's first director. Campos quotes him as saying: "the principles of evolution will show the way to an improvement of the human race," while also highlighting "how organisms may be best modified to meet our requirements of beauty, food, materials and power" (Davenport quoted in Campos 2009: 7). Such a drive to control and modify organisms to serve human ends, a drive that now underlies synthetic biology, has therefore long played a significant role in biology. With many already believing, over a hundred years ago, that the answers to the question 'what is life?' was to be discovered through synthesis not analysis (Keller 2002).

Keller's book *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines*, for example, provides a fascinating account of some of the most significant attempts that have been made since the beginnings of the twentieth century to synthesise life. For some, such as Leduc, this took the form of producing artificial life, while others focused on the similar sounding, but significantly different, artificial production of life.

One of the most noteworthy early examples of this second approach was the work of Jacques Loeb, the first person to induce parthenogenesis[146] (Loeb 1913).

Loeb was, according to his biographer Pauly (1987), the foremost public advocate of an engineering approach to biology between 1890 and 1915. Expressing his adherence to such an approach in a letter to physicist Ernst Mach in 1890, Pauly quotes Loeb as writing, "[t]he idea is now hovering before me that man himself can act as a creator even in living nature, forming it eventually according to his will. Man can at least succeed in a technology of living substance" (Loeb quoted in Pauly 1987: 51). Moreover, it was not only the creation of living nature that Loeb saw as the future of biology, but its control. To this ends he wrote, in the preface to *Studies in General Physiology*, "it is possible to get the life-phenomena under our control, and that such a control and nothing else is the aim of biology" (1905: ix). Yet, despite such claims, claims which would not seem out of place in present day synthetic biology, these earlier incarnations of synthetic biology met with significant resistance from many biologists.

Benjamin Gruenberg wrote in 1911, "[v]ery few of the attempts to produce 'artificial life' have been made by biologists, who realize too well the complexity of the problems involved" (1911: 231). Indeed at the time Gruenberg wrote this, and for many years afterwards, many of those who attempted to create artificial life, artificially create life, or indeed explain life, using concepts from physics, engineering, and mathematics, hailed from the physical sciences or mathematics. Much like the engineers who first fomented the modern idea of synthetic biology, but without the collaboration of biologists. As such, Keller (2002) reports, their efforts encountered significant resistance from biologists. Take for example D'Arcy Wentworth Thompson, Nicolas Rashevsky, and Alan Turing, all of whom proposed the application of

[146] Parthenogenesis is a type of asexual reproduction in which offspring develop from unfertilised eggs. In 1899 Loeb artificially induced such reproduction in sea urchins by altering the chemical content of the water in which the eggs were kept.

mathematics to biology in order to explain biological processes and structures. While Thompson was himself a biologist, his attempts, like those of mathematicians Rashevsky and Turing, were roundly discounted by biologists as being oversimplified (Keller 2002). Many biologists, Keller explains, were resistant to the idea, represented by such attempts, that science needed to be mathematical. Viewing mathematical modellers as arrogant, ill-informed intruders into biology (Keller 2002).

This general resistance from biologists to the idea of collaboration with engineering was arguably significant. For, despite the steady influx of mechanistic ideas and concepts into biology, and the incremental shifts in biology towards the concepts and approaches of engineering, there was not enough perceived underlying unity between the two fields, at this time, to allow for their convergence. This then raises the question, what has changing in the intervening years to make such a convergence now possible? The answer, I suggest, can be found in the continued, though gradual, social and technological shifts outlined below.

Nevertheless, despite the claims from the BMJ (1910) regarding biology being poised to enter its synthetic phase, what is interesting about the attempts at applying ideas from mathematics and engineering to biology, that Keller (2002) addresses, is that their primary aim was analytical. They were, that is, largely geared towards understand more about biology and life itself rather than towards controlling it. Indeed, even Loeb recanted his claims about controlling life. Determining, in his later years, that scientists "could do only one, rather passive, thing: to look at nature and try to see the hidden mechanisms underlying biological processes" (Pauly 1987: 130). However, as Campos (2009) addresses, others from within biology were more inclined to embrace the stance expressed in Loeb's earlier conviction. Clinging to the belief that biology could be, and should be, manipulated and controlled. An approach that has, I would contend, ultimately led to synthetic biology.

Campos (2009) writes that this trend began in the early twentieth century amongst agriculturalists, breeders, and geneticists. Biologists, that is, who embraced the idea of experimenting with evolution in order to improve species and varieties. Campos (2009) draws out several particular examples to illustrate this trend, including Thomas Hunt Morgan, and Albert F. Blakeslee.[147] Morgan started the *Drosophila* school of genetics at Columbia in the 1910s-20s to study mutations (Campos 2009), while Blakeslee reportedly established the production of "synthetic new species" (2009: 13) using chromosomal mutations, in the 1920s and thirties. Campos quotes Blakeslee as describing these "synthetic" species as being "made up to order, as it were, with definite plan and purpose" (Blakeslee quoted in Campos 2009: 13). Microscopes were central to this interventionist work, allowing as they do, greater understanding of cell structure and function. Thus, the drive to manipulate organisms was accelerated in the 1930s by the development of electron microscopes, which were capable of far greater resolution and magnification than their predecessors, the light microscopes (Marton 1968). Furthermore, in permitting the visualisation of the macromolecular structure of biological cells, these microscopes not only advanced the interventionist approach to biology, moving biology closer to the current point of convergence with engineering, but they also paved the way for the development of molecular biology.[148]

Molecular biology

Kay (1993) writes that in 1938 the then director of the Rockefeller Foundation's natural science division, Warren Weaver, coined the term 'molecular biology.' He reportedly did so in order to capture the centre's increasing focus on the "ultimate minuteness of biological entities" (1993: 3). Yet, despite the continuity of the name, Kay (2000) stresses that what is thought of as molecular biology today, is not what was encompassed under the term in the 1930s and forties. Rather, at this time the discipline was narrowly focused on macromolecules. It was also heavily influenced by two

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[147] Blakeslee was the second director of the Station for Experimental Evolution.

[148] Molecular biology, at the time, focused its study at the sub-microscopic level (10^{-6} and 10^{-7}cm) which is the region between molecules and cells (hence the focus on macromolecules) (Kay 1993).

key elements of the notion of life as organisation, namely specificity and the protein paradigm (Kay 2000).[149]

With similarities to Compton and Bunker's (1939) contemporaneous vision for biological engineering, Kay writes that Weaver[150] envisioned molecular biology as a "new interdisciplinary biology . . . grounded in theories and technologies of the physical sciences" (2000: 45). Following such an approach, the aim of molecular biology was to discover the underlying physiochemical laws governing vital phenomena. This goal was to be achieved by looking at life processes and organisation, rather than the host organisms themselves. A change in focus that ultimately expanded the mechanistic understanding of life, as not only organisms, tissues, movements, and cells came to be understood in mechanistic terms, but also life's processes. Furthermore, this shift in focus from the 'whole' to the 'parts,' spelt the beginnings of the move away from the notion of life as organisation, and a step closer to the advent of 'parts'-focused approaches like that of synthetic biology.

Molecular biologists removed all considerations of biological and environmental context[151] from their study of life and became much more interested in the common phenomena of life, such as reproduction, than they were in diversity. As it was easier to study these common phenomena in simple biological systems, bacteria and viruses were employed to act as models for more complex systems and organisms (Kay 1993). A situation which Kay argues led to Jacque Monod's infamous dictum that "what is true for the bacterium is true for the elephant" (Kay 1993: 5). Furthermore, given

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[149] The protein paradigm held that the processes of life could be explained through the structure and function of proteins. While specificity, the primary biological concept within the notion of life as organisation, denoted "the complementarity of highly ordered biological structures" (Kay 2000: 41) and the remarkable functional specificities within biological entities, whilst drawing heavily on the lock and key metaphor.

[150] Who was himself a mathematical physicist.

[151] For example the emergent properties of the organisms, and the interactive processes occurring within organisms, between organisms and between organisms and their environment.

their focus on model organisms and the specificity of macromolecules, molecular biologists came to require complex and sophisticated apparatus.

Kay (1993) subsequently argues that the introduction of massive and sophisticated apparatus into biology not only turned biological laboratories into the technological landscapes they are today, but was significant in several other key ways. She writes that such scientific instruments "are not mere devices for discovering objective reality but complex processes of intervention for representing nature, processes that alter nearly all aspects of scientific practice" (Kay 1993: 7). Thus molecular biology came to reify the molecular level as the essential locus of life. Making "the representation of life contingent upon technological intervention" (Kay 1993: 8). This growing technologisation of biology, and of our understandings of life, has been, I would argue, significant in the movement towards the current crossroads of biology and engineering. Indeed, I would argue that, the increasing encroachment of the technologisation and mechanism that underlie engineering, into the study of life and biology, has been instrumental in the emergence of engineering-inspired fields such as synthetic biology.

Nevertheless, whilst this interventionist approach to biology remained, and continued to gain dominance, the 1940s and fifties saw a significant reshuffling of ideas and techniques. The concept of a genetic code was introduced, the structure of DNA was discovered and, as a result, the protein paradigm was ousted and specificity dethroned. When the dust cleared from all of this upheaval, biology had taken further steps towards the intersection with engineering, and the concept of life as organisation had been replaced with that of life as information.

Life as information

Kay (2000) argues that in the post war years, the narratives of heredity and life within molecular biology, and the idea of organisation, were recast as programmed communication systems. Thus, just as the widespread adoption of the theory of mechanism had aligned the natural and physical sciences during the Scientific Revolution, the adoption of information theory aligned molecular biology with other contemporary scientific disciplines within, what Kay (2000) terms, the cold-war technoculture.[152] Central to this 'technoculture' was the burgeoning relationships between science and technology, thus biology's adoption of language and concepts drawn from technology, particularly computing, again moved the field closer to engineering.

The shift towards the concept of life as information was famously solidified following Watson and Crick's ground breaking 1953 discovery of the structure of DNA.[153] After which Crick, who went on to become a theoretical molecular biologist,[154] played a central role in formalising the discourse of linguistics and information theory within biology.[155] Words such as code, information, and message, all drawn from information theory and prevalent in computing,[156] began to appear with increasing regularity in the discourse of biology (Kay 2000: 53). As Kay writes, "biological specificity became informational, and information, message, and code eventually became biological concepts"

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[152] Another significant shift towards the notion of life as information came at the expensive of specificity. In light of the information theory filtering into biology, specificity came to be seen as limited in its ability to explain life. It was, according to Kay, considered "immobile and grounded in matter" whereas its replacement 'information,' "came to serve as its carrier beyond material bounds . . . possessing motion, information could transcend the limits of structure. Specificity was mute; information communicated specificity's messages" (Kay 2000: 41).

[153] Jacob (1973) writes that in the 1940s Austrian radiation biologist Henry Quastler became the first person to attempt to develop information theory within biology. Quastler was determined to turn molecular biology into an information science, and thus reportedly strove to rework biochemical specificity (the central concept of life as organisation), in favour of information theory; to shift the discipline's focus from biology's material and structural properties to its nonmaterial attributes. Yet, Jacob (1973) notes, despite his enthusiasm Quastler encountered enormous difficulties in actually applying information theory quantitatively to biology, and thus he ultimately abandoned his attempts. After the end of WWII, however, things began to change as 'information' came to be seen as both a physical parameter and a precisely defined concept that could be studied (Kay 2000).

[154] Francis Crick was a doctoral student when he and James Watson discovered the structure of DNA, completing his PhD in 1954. After completing his PhD his work focused on the 'information flow' from DNA to proteins (Crick et al. 1961; Crick 1970; Olby 1970).

[155] Francis Crick played a significant role in the development of the notions of the Central Dogma and of the genetic code.

[156] Which, as mentioned previously, was the predominant mechanistic analogy for life in the twentieth century (Nicholson 2013).

(Canguilhem 2000).[157] Kay (2000) notes that in the 1950s, molecular biologists sometimes used quotation marks when they employed terms such as 'information' and 'code,' as a way of acknowledging their metaphorical and heuristic dimensions. However, by the end of the decade these quotation marks disappeared as the linguistic tropes of the new biosemiotics became naturalised. Indeed, Kay maintains, that it became "virtually impossible to think of genetic mechanisms and organisms outside the discursive framework of information" (2000: 39).

This naturalisation of both the 'life as information' discourse, and the casting of molecular biology as an information system, occurred despite many, including information theorists, cryptologists, linguists, and life scientists, questioning its appropriateness (Kay 2000). This, Kay contends, was in large part due to two key factors. The first of which was the cultural resonances of the informational and scriptural representations in the post-war period. "The notion of 'code,'" Kay writes, "carried multiple historical allusions and contemporary referents, eliciting imagery of transcendent knowledge, Mosaic tablets, positivists' ideals of nature's laws, secret writings, period intrigues and espionage and cryptology, ideas from linguistics, information theory, and cybernetics" (2000: 14). The second of these factors was the efficacy of the models and analogies for biological meaning that these representations provided. 'Information,' 'language,' 'code,' and 'message' are, Kay (2000) concedes, compelling and productive as analogies for biological meaning making. However, she maintains, that they have erroneously been taken as ontologies.[158]

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[157] Yet, as Canguilhem addresses, the concept of life as information did not account for where such biological information originated. Thus Canguilhem raises the question, "How did the first self-organization come about if communication depends on a prior source of information?" (2000: 88).

[158] Kay (2000) writes that Austrian physicist Erwin Schrödinger's 1944 book *What is Life?* was very influential in the eventual shift towards the concept of life as information. In it, Schrödinger draws on the analogy of Morse code to propose the idea that a code-script could account for biological complexity and specificity. Yet, while Kay writes that he is attributed with being the "progenitor of the genetic code" (2000: 59), Schrödinger's concept did not involve the transfer of information. As such his code was not 'the code,' but it did help pave

Yet, over the subsequent fifty years or so, this change in discourse not only signified a new way of speaking about biology, but also came to signify a new way of thinking about, and interacting with, biology. Life came to be seen as mechanistic at the most fundamental level yet, that of the DNA, the machine code for the organismic 'computer' if you will. As such, the human genome, viewed as an information system, became the software, or the 'Book of Life,' which was to be read and, some thought, could be edited (Kay 2000; Pollack 1995). As Canguilhem wrote in 1966, regarding the shifts in biology following 1953, "[t]he science of life no longer resembles a portrait of life, as it could when it consisted in the description and classification of species; and it no longer resembles architecture or mechanics, as it could when it was simply anatomy and macroscopic physiology. 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" (Canguilhem 2000: 317).

However the aim was not simply to understand life, but also to control it. Derrida (2013), for example, wrote of the way representing nature had become intertwined with the drive to intervene in nature, as the idea of reading the 'book of life' became inseparable from the act of writing it. This shift, Kay contends signified "an emergent form of biopower, as the material control of life would be now supplemented by the promise of controlling its form and logos, its information (the DNA sequence, or the 'word')" (2000: 3). This is a clear embrace of the same goal that initially consumed Loeb. However in the intervening years many technological advances have been made to render

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the way for the subsequent elucidation of the genetic code. Between the publishing of Schrödinger's book and 1953 at least three scientists, Stern, Hinshelwood, and Dounce, also tried to explain the combinatorial properties of biological codes (Kay 2000). The first step towards this goal was the discovery of the structure of DNA, a feat that was quickly followed by the explication of the structure of codons and of the genetic code itself. Physicist George Gamov was the first to propose a code involving nucleotide triplets, and while his formulation was incorrect, it did influence the successful 1961 formulation of Francis Crick and his colleagues (Crick et al. 1961; Hayes 1998). The rest of the genetic code was elucidated by Har Gobind Khorana (1968) and his team.

biology more susceptible, though as chapter five outlined, not completely susceptible, to such control.

Kay (2000) thus notes that, the increasingly interventionist and technological approach to studying and representing life was believed, in the latter half of the twentieth century, to finally, and truly mark the end of biology as an analytic form of inquiry and its beginning as a synthetic science. Furthermore, unlike the 'synthetic biology' of Loeb, Leduc, and their contemporaries, with the advent of modern biotechnology, the role of 'synthesising' biology shifted from being primarily a way to understand life, to being a method for producing desirable bio-products.

Modern biotechnology

The interwar years thus not only saw the beginnings of molecular biology, but also a major advance in biotechnology, as it came to be associated with the application of biology to humanity.[159] An early major success of this modern biotechnology was Penicillin. Discovered in 1928 by biologist, Alexander Fleming, it was not until the 1940s that its ability to treat infection was thoroughly appreciated. Yet Ford (2014) notes that producing it in sufficient quantities was a major problem, especially given the escalating number of

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[159] The origins of biotechnology go back, if not to the ancient Egyptians, then at least as far as 1828. At this time Jean-Jacques Virey, developed the influential idea that "man has had to develop technology to make up for the loss of natural instincts" (Bud 1993: 54). He termed this innate human trait 'biotechnie' and argued that tool making was a biological phenomenon. As such he used 'biotechnie' to argue that all of engineering is co-opted as a subset of biology. This usage differs markedly from later coinages of similar words, and from our current understandings of it, however it influenced Bergson to develop the notion of '*homo faber,*' ('man' the maker). Another early coinage of 'biotechnology' came from Gustav Tornier at the World Zoological Congress in Berlin in 1901. Tornier, noting that many papers addressed analogies between biological and mechanical systems, proposed that the category of "technology" could be applied to living organisms in general, he termed this 'bionten.' He also proposed that the process of modifying or using living organisms technologically be termed 'biontotechnik' (Bud 1993). However Bud writes that such early biotechnology was restricted to the production or processing of food products, sewage, and beer. Thus it wasn't until the interwar years that biotechnology acquired a new association, one that revolved around the application of biology to humanity. The focus of this new branch of biotechnology was on health, eugenics, nutrition, and non-polluting manufacturing technology that utilised renewable natural resources. In the 1930s this 'idealistic' branch of biotechnology came together with the industrialised zymotechnic (the study of yeast fermentation) branch to form a 'new' and 'modern' biotechnology (Bud 1993).

cases of serious infection generated by World War Two. Chemical engineer Margaret Hutchinson Rousseau eventually derived a solution to this production problem by drawing on the processes of zymotechnology to design a system of deep tank fermentation for Penicillin's first production plant. This solution, Ford (2014) writes, ultimately allowed for sufficient quantities of Penicillin to be ready for the Allied troops before the 1944 invasion of Normandy. Thus its production was undoubtedly an important achievement for medical care, and a significant milestone for biotechnology. However it was also a significant milestone for the role of engineers in the life sciences. Given that, the episode highlighted the importance of both engineers and biologists in the success of modern biotechnology.

Franklin (2000) writes that, with the advent of modern biotechnology, and its focus on 'reprogramming' and 'reorganising' biology in order to produce biotechnical objects, the interventionist approach to biology gained momentum. A central part of this strategy, discussed in-depth by Hannah Landecker (2007), was the emphasis placed on biological plasticity. Drawing on the work of Loeb and H.G. Wells[160] Landecker writes, "[p]lasticity is the ability of living things to go on living, synthesizing proteins, moving, reproducing, and so on despite catastrophic interference in their constitution, environment, or form" (2007: 10). This capacity to alter cells, to alter biology in such a purposeful way has, Landecker contends, allowed biotechnology to progress, as without it experimentally altered organisms would simply die (Landecker 2007).

Biological plasticity is thus a scientific requirement for the production of biotechnological entities. However, as Ladisch (2004) points out, it is not the only requirement for the success of biotechnology. The other key factor in the advancement of biotechnology being the design and production of equipment

[160] H.G. Wells was critical of the fatalistic nature of hereditary thinking, believing instead that living matter was highly malleable and thus could be moulded and modified by humans. This approach to biology was adopted by the character of Dr Moreau in Wells' book *The Island of Dr. Moreau*, in which Wells questions the difference between partly man-made organisms and naturally occurring ones (Landecker 2007).

and processes to turn these entities into commercial products. This part of the work is not done by biologists, but rather by engineers like Margaret Hutchinson Rousseau, and is referred to as bioprocess engineering. Where The United Nations Convention on Biological Diversity defines biotechnology as, "[a]ny technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use" (United Nations 1992: Article 2, Use of Terms), Ladisch writes that it is bioprocess engineering that puts biotechnology to work. It is, he claims, the bioprocess engineers who design and develop the equipment and processes required by biotechnology in order to "generate bioproducts in large volume, at low cost, and with acceptable purity" (Ladisch 2004: 29).

In the 1970s, this combination of biological plasticity and bioprocess engineering allowed modern biotechnology to come into its own, spurred in large part by the invention of recombinant DNA technology[161] (S. S. Hughes 2011). This, now universal, form of genetic engineering[162] extended the power and scope of molecular biology, becoming the cornerstone of what would become the biotechnology industry. Though the field was arguably ready and waiting for such a revolutionary invention to move it forward. In 1972, a year before recombinant DNA technology was invented, Wright (1994) notes that the head of the Center for Theoretical Biology at the State University of New York, James Danielli, "anticipated an 'age of synthesis' in which molecular biology would be applied in the creation of organisms tailored to carry out specific tasks in industry and agriculture – for example, bacteria to manufacture chemicals or digest pollutants and plants to fix nitrogen from the air" (Wright 1994: 69). Two years later, Waclaw Szybalski echoed Danielli's

[161] Recombinant DNA technology allows for the combination of strands of DNA from two or more species and for the replication of any specific DNA sequence.

[162] Luis Campos (2009) writes that while recombinant DNA technology is now considered to be genetic engineering, in the early 1970s such techniques were often referred to as 'synthetic biology' as the term 'genetic engineering' was perceived by some to carry eugenic connotations. However, by the mid-1970s the name 'synthetic biology' disappeared from use again and 'genetic engineering,' shaking off any remaining resistance, rose to prominence.

(and indeed the much early BMJ's) anticipation of biology's "age of synthesis," writing:

> "Let me now comment on the question 'what next.' Up to now we are working on the descriptive phase of molecular biology. . . . But the real challenge will start when we enter the synthetic biology phase of research in our field. We will then devise new control elements and add these new modules to the existing genomes or build up wholly new genomes. This would be a field with the unlimited expansion potential and hardly any limitations to building 'new better control circuits' and . . . finally other 'synthetic' organisms, like a 'new better mouse'. . . . I am not concerned that we will run out of exciting and novel ideas, . . . in the synthetic biology, in general" (Szybalski 1974: 405).

The excitement and anticipation expressed by Danielli and Szybalski is unsurprising given the successes this interventionist approach to biology was having in the 1970s, as biology began to be synthesised and manipulated at the genetic level. Both the first complete gene (H. G. Khorana et al. 1972) and the first recombinant DNA molecules (D. A. Jackson et al. 1972), were synthesised in 1972. A year later came the first transgenic organism (Cohen and Chang 1973) and then a year after that, the first transgenic animal (Jaenisch and Mintz 1974). By 1981 the first peptide-coding gene (Itakura et al. 1977), and the first protein-coding gene (Edge et al. 1981), had also been synthesised.[163] While these milestones were significant for the advancement of knowledge in molecular biology, and are arguably predecessors to synthetic biology's

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[163] It was not however until thirty years after Danielli's prediction that the first virus was synthesised (Cello et al. 2002). Then, more recently, the first genome (Gibson et al. 2008), and the first so-called 'synthetic organism' (Gibson et al. 2010). As discussed in chapter five, there is much debate over whether the resulting organism of this experiment was indeed 'synthetic.' However, regardless, the experiment is widely considered to be an important step forward in the synthesis of biology. While these three more recent milestones are frequently included under the banner of the current incarnation of synthetic biology, they clearly have links with their predecessors, and all of them can be thought of as the results of modern biotechnology.

'Synthia' and syn3.0, they were also significant for the commercial advancement of biotechnology.

Indeed, three years after the invention of recombinant DNA technology one of its inventors, Herbert Boyer,[164] formed Genentech,[165] the first biotechnology company. At the time of Genentech's emergence, in the mid 1970s, Hughes writes that molecular biology was becoming "practical, profitable, and controversial in a manner never before experienced" (2011: 112). This was a significant shift for biology away from a focus on the production of knowledge and towards a focus on the production of industrialised and commercialised products. Such a focus is more often associated with engineering, and is, as discussed previously, clearly evident in synthetic biology. In keeping with this shift in the culture of biology, Genentech's aim, Hughes (2011) contends, was to use recombinant DNA technology as an industrial process. In order to engineer bacteria to produce insulin, growth hormone, and other important pharmaceuticals, which could be used as commercial products.

Through much hard work they managed to show that chemically synthesised DNA could be introduced into bacteria, which could act as a biological 'factory' to produce biologically functional proteins (S. S. Hughes 2011). This, Hughes (2011) argues, was revolutionary both scientifically and commercially, with Genentech becoming the overnight darling of Wall St when its public stock offering, four years after the company formed, saw the largest gain in stock market history (S. S. Hughes 2011).[166] Such successes as that of Genentech, thus led Andrew Hacking (1987) to write that biology is

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[164] The other inventor of Recombinant DNA technology was Stan Cohen. For an account of its invention and the formation of Genentech see Hughes (2011).

[165] The name Genentech was a contraction of genetic engineering technology.

[166] Share prices rocketed from $35 to $89 in the first few minutes of trading. Yet, while Genentech blazed a trail that many other young companies followed, quickly bringing the biotechnology industry to life, by 1985 progress had already begun to slow. It was, as both Genentech and their competitors discovered, surprisingly difficult to realise the novel and complicated pharmaceuticals that were required for future marketable products (S. S. Hughes 2011).

now considered a manufacturing technology, a means to production for biotechnology.

These advances within biotechnology are significant to the history of synthetic biology, as they not only paved the way for biology to be used as a manufacturing technology, but they also saw biologists and bioprocess engineers working together to achieve this ends. Ladisch (2004), for example, writes in regards to Genentech's production of human insulin, that it was engineers who designed the process to recover and purify the insulin once biologists had figured out how to produce it. Ladisch (2004) also notes that bioprocess engineers were involved in the Human Genome Project, designing the automated instruments and the software for analysing nucleic acid sequencing as the biologists worked in the laboratories. However, while these are undoubtedly important functions, and the engineers who perform them are undeniably integral to the process and progress of biotechnology, the role of engineers within this sort of biotechnology was arguably a supporting one to the biologists.

Nevertheless, I would argue that the biotechnology and molecular biology of the twentieth century did finally move biology out of, what the BMJ (1910) termed its analytical phase, and into the beginnings of its long anticipated synthetic phase. I would also contend that modern biotechnology has, with its reliance on both biologists and engineers with a common goal and an eagerness to work together, helped to bring the two fields up to a point of disciplinary convergence. Furthermore, I would argue that the results of this convergence, and this emphasis on synthesis, are now playing out in a new way of 'doing' and thinking about biology in this new century. A shift that has, in part, filled the gap left by the decline of the notion of life as information in the wake of the Human Genome Project.

The limits of life as information

Launched in 1990, the Human Genome Project was the world's largest collaborative biological project. Following the elucidation of the genetic code in 1953, the drive within molecular biology shifted towards determining the codes and contents of entire genomes. This work, Keller notes, started with simple organisms,[167] and cemented the idea that genes, and their sequences, were responsible for all biological function. Thus, it came to be believed that "sequence information would, by itself, provide all that was necessary for an understanding of biological function" (Keller 2000: 6). As such, determining the human genome would, it was hoped, allow us to link all genes to their functions and establish which single, or small number of, mutations were responsible for which diseases.

After thirteen years of international work, the results of the Human Genome Project were published in 2003. While these results were fascinating they were not what many had anticipated. Given the complexity of humans, and the size of the previously determined genomes of simpler organisms, it was anticipated that the human genome would contain between 100000 and 300000 genes. However, when the results were published it became clear that the genome contained only 20000-25000 protein coding sequences (N. Rose 2007). Thus the 'gene for' paradigm[168] fell by the wayside as it became apparent that "the human genome could not be the 'digital parts list' for making a human being" (N. Rose 2007: 46). The genome was not the blueprint of life people were expecting. Furthermore, the unpredicted results of the Human Genome Project resulted in the tacit acknowledgement of "how large the gap between genetic 'information' and biological meaning really is" (Keller 2000: 8). Life's secrets, Keller (2000) stressed, have been shown to be far more complex than previously imagined, and this complexity cannot be captured by the informational epistemology.[169]

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[167] The first genomes to be determined were those of a bacteriophage with an RNA genome (Jou et al. 1972) and a bacteriophage with a DNA genome (Sanger et al. 1978). These milestones were achieved in the 1970s, but it would be another twenty years before the first bacteria genome (Fleischmann et al. 1995), archaeon genome (Bult et al. 1996), and eukaryotic genome (Goffeau et al. 1996) were completed.

[168] The 'gene for' paradigm is the notion that there is a single gene, or a small group of genes, responsible for each biological feature and function.

[169] Following the findings of the Human Genome Project, the central dogma (that there is a one-way path from DNA to RNA to protein) can no longer be sustained, and areas of DNA that do not code for proteins (more than 98% of the genetic material in our cells) previous

Thus, while information theory continues to provide biology with much of its discourse and concepts, since the beginning of the 21st century the way in which biology is described, understood, and undertaken appears to be shifting once more. Keller quotes François Jacob as writing in 1973 that, "[t]oday the world is message, codes and information. Tomorrow what analysis will break down our objects to reconstitute them in a new space?" (Jacob quoted in Keller 2000: 8). For some, this new analysis has taken the form of a post-genomic emphasis on biological complexities, complexities which cannot be captured by the informational epistemology (Keller 2000). Integral to this focus is a shift in emphasis away from the gene.[170] A shift that Nikolas Rose addresses when he writes, "the focus shifted from the gene to processes of regulation, expression, and transcription (transcriptomics), from the gene to those small variations at the level of a single nucleotide termed Single Nucleotide Polymorphisms (SNPs), and indeed from the gene to the cell and the process for the creation of proteins (proteomics)" (2007: 46). Part of this shift in emphasis, and a prime example of a post-genomic field of study is epigenetics.[171]

While such post-genomic attempts to do biology differently are focused on basic science, the other major emergent trend within biology, which I shall

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termed 'junk DNA' has been found to actually be crucial for regulation. As such a lot has been discovered that makes the informational model of DNA as the 'book of life,' seem untenable (Rose, 2007).

[170] Indeed Keller (2000) writes that the twentieth century was the century of the gene, and that the gene's dominance ended with the turn of the century.

[171] Although it was first posited as a way of reuniting developmental biology and genetics in the mid-twentieth century, epigenetics only really emerged as a discipline in the first decade of the twenty-first century once the limitations of the Human Genome Project were widely known (Goldberg et al. 2007). This relatively new field of study analyses the impacts of external and environmental factors on the gene expression and phenotype of an organism (N. Carey 2012). This focus on how our environment, and indeed the environment experienced by our parents, and even grandparents, influences our biology, as Bird (2007) discusses, is being seen by some as a potential antidote to the genetic determinism so dominant in the twentieth century. It is also hoped that epigenetics, and the epigenome, once it is eventually elucidated, will fill in many of the knowledge gaps left by the Human Genome Project (Holliday 2006), and thus further our understandings of life. See Huang (2000) for a further discussion of post-genomic biology.

discuss below, has instead taken the drive towards biological synthesis and convergence between biology and engineering to a new level. That is, where the post-genomic fields are focused on furthering our understanding of biology and life, the trend I explore here, which encompasses synthetic biology, has opted to side-line the desire to understand life. Focusing instead on manipulating and controlling it using concepts, language and tools from engineering. It is a trend that is emerging at the crossroads of biology and engineering and one that appears to be reformulating the conception of life, replacing life as information with life as engineerable material.

Life as engineerable material?

As discussed above, the notion that ideas and methods from engineering could be, and should be, applied to biology is far from a new one. However, building on the advances in molecular biology and biotechnology, these ideas seem to be gaining more and more traction in recent years. In 2000 Keller wrote that twentieth century geneticist H.J. Muller "imagined the prospect of controlling genetic change in ways that would 'place the process of evolution in our hands'" (Muller cited in Keller 2000: 141). Looking forward into the twenty-first century, Keller states that Muller's "fantasy has come to look more and more like a realizable prospect" (Keller 2000: 141), and that a key step towards realising such a fantasy was the enlargement of genetics' "conceptual toolkit" using concepts and terms from engineering. She wrote:

> "Engineers have developed a conceptual toolkit for the design of systems – like airplanes, for example, or computers – in which reliability is the first and foremost criterion. As such, their approach might be said to be directly complementary to that of geneticists, and I suggest that the latter might profitably borrow some of the concepts and terms developed in the study of dynamic stability to enlarge their own conceptual toolkits" (Keller 2000: 147).

While Keller is arguably correct, sixteen years on, geneticists are not the only 'biologists' now 'profiting' from the introduction of engineering concepts and tools. Instead, much like Quastler's attempts to turn biology into an information science, new collaborative groupings of biologists and engineers, like those within synthetic biology, are attempting to draw from the framework of engineering in order to reformulate how we think about and 'do' biology in different areas. Prime examples of such hybrid, emerging disciplines and research communities are, neuro-engineering (Eliasmith and Anderson 2004; He 2013), nanobiotechnology (Klefenz 2004; Lowe 2000; Niemeyer and Mirkin 2004), tissue engineering (Langer and Vacanti 1993; Lanza et al. 2011; Viola et al. 2003) particularly with the use of 3D bioprinting (Doyle 2014; Wang et al. 2015), genome engineering (Carr and Church 2009), particularly with the use of CRISPR (Hsu et al. 2014), the proposed synthetic human biology consortium[172] (Boeke et al. 2016; Callaway 2016), and of course the discipline I have focus on here, synthetic biology.[173]

While it is arguably clear how such hybrid fields have arisen out of the recent advances in molecular biology and modern biotechnology, it has been my aim in this chapter to outline how the trend towards seeing life in mechanistic, reductionistic terms goes back much further. Indeed the strands of thought and approach, which define synthetic biology and its ilk, have their roots in the various preceding conceptions of, and approaches to studying, life outlined above. The mechanistic conception of organisms, the notion that organisms can be thought of and treated as factories, the desire to control and manipulate biology, the shift in focus from analysis to synthesis, the disregard of biological and environmental context. All of these factors are central to the

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[172] The synthetic human biology consortium is a proposed public-private initiative to synthesise an entire human genome from scratch. The effort is being called the 'Human Genome Project – write' to distinguish it from the previous human genome project which focused on 'reading' the genome. It is anticipated that the effort could well take a decade given that, at present, only tiny bacterial genomes have successfully been synthesised from scratch. However it is facing resistance both within and outside of the synthetic biology community, as questions are being asked about the ethics of such an endeavour.

[173] While it is synthetic biology that I am focusing on in this thesis, it is worth remember that it is far from the only example of the shifts I describe in this and previous chapters.

conception of life as engineerable material, and all arose, as outlined above, long before the likes of modern synthetic biology.

As such it is understandable that synthetic biology, and most of these other fields, may appear at first glance to be nothing more than new branches of biotechnology. They do, after all, rely on and exploit biological plasticity as they strive to make biotechnical products, and they do aim to scale these processes up in order to produce commercial products. Yet, while they fall under the umbrella of biotechnology, there are nonetheless significant differences between synthetic biology and its ilk and the biotechnology and molecular biology that preceded them. Differences, which ultimately set these fields, and their conception of life, apart from the approaches to thinking about and 'doing' biology which preceded them. In terms of synthetic biology, Heinemann and Panke highlight that where molecular biology has "attempted to unravel the molecular mechanisms that are important in cellular function" and "biotechnology has exploited this knowledge and adopted some of these mechanisms to produce chemicals, enzymes and biopharmaceuticals," by contrast synthetic biology is "adopting a very ambitious agenda in building novel biological entities on an ever more complex level for novel applications" (2006: 2797).

What this equates to is, rather than simply drawing on the work of engineers to design and build equipment and bioprocesses,[174] these emerging disciplines are drawing on ideas, methods, and discourse from engineering. Incorporating what has been called an engineering approach, into the study and conception of biology. As discussed in chapter four, synthetic biology does not just view the processes and equipment used in biology as engineerable, but also, at least rhetorically, the organisms and biological entities themselves. Renowned for its parts based approach to biology[175, 176] (Endy 2008), synthetic

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[174] This was the case in earlier incarnations of biotechnology, and indeed still is the case in many branches of biotechnology.

[175] The notion that a functioning biological entity could be designed and built using standardised, characterised, and engineered BioBrick parts and devices which have their sequences effectively black boxed (Endy 2008).

biology is considered to be a "transformative innovation that will make it possible to build living machines from off-the-shelf chemical ingredients, employing many of the same strategies that electrical engineers use to make computer chips" (Tucker and Zilinskas 2006: 25). Where genetic engineering involves the transfer of individual genes from one species to another, synthetic biology "envisions the assembly of novel microbial genomes from a set of standardized genetic parts" (Tucker and Zilinskas 2006: 26).

While syn3.0 highlights that such genomes cannot, as yet, be completely assembled using only standardised, well-characterised parts,[177] the confidence and commitment that underlies the engineering approach persists. Thus, even without the realisation of this engineering ideal, organisms with semi-engineered genomes are being utilised to produce products. Furthermore, such semi-engineered organisms (organisms which would arguably fall within the boundary spanning category proposed in chapter five), are not solely being employed to produce 'classic' biotechnical products such as pharmaceuticals,[178] foodstuffs,[179] cosmetic additives,[180] 'plastics,'[181] textiles,[182]

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[176] Which bears conceptual similarities with the notion of interlocking components central to the conception of life as organisation.

[177] Requiring, as they do, a fair number of genes whose function is unknown in order to produce organisms that can survive and reproduce, and thus perform their desired functions.

[178] Such as Artemisinin, an antimalarial drug, which in 2014 became the first synthetic biology pharmaceutical agent (Paddon and Keasling 2014).

[179] For example vannilin, a synthetic vanilla flavour, which was the first synthetic biology food additive to reach market (E. C. Hayden 2014). Evolva, the company which produces vannilin, is also working on synthetic biology versions of saffron and Stevia (Barras 2014).

[180] Valencene, which produces the aroma of oranges (Barras 2014) and nootkatone, which produces the aroma of grapefruit (E. C. Hayden 2014), are both produced by engineered yeast, and both are used in perfumes and cosmetics

[181] Mirel, for example, is a bioplastic made by an engineered microbe turning corn sugar into plastic polymer (Church and Regis 2012)

[182] For example Bio-PDO, a biologically-derived version of the chemical 1,3-propanediol produced by engineered *E. coli* . Bio-PDO is the main ingredient in the DuPont fibre Sorona, used in carpets, upholstery and clothing (Church and Regis 2012).

and biofuels.[183] But rather, biological 'machines' with a wide variety of traditionally mechanical, rather than biological, functions, are also being produced. Functions such as, the expression of Boolean logic, the ability to take 'photographic' images, and the production of programmable platforms (Endy 2008).

Moreover, while Loeb proposed similar ideas about the engineerability of biology over one hundred years ago, and genetic engineering is named after the field, these earlier incarnations of an interventionist approach to biology involved no engineers and little in the way of engineering (Baker et al. 2006; Chopra and Kamma 2006). As mentioned above, biologists, mathematicians, and physical scientists were largely responsible for the earliest attempts to design and control biology, not engineers themselves, and many of these attempts met with resistance from the biology community. Even in molecular biology and biotechnology, where the work is primarily done by biologists, engineering is used as an analogy for the rational combination of genes (de Lorenzo and Danchin 2008). While the bioprocess engineering that is done is focused on the equipment and processes, not the organisms themselves.

By contrast, synthetic biology ostensibly views engineering as "a veritable methodology with which to construct complex biological systems from first principles" (de Lorenzo and Danchin 2008: 822) and it is engineers themselves who are applying this methodology. This then is a field that is currently poised at the crossroads of biology and engineering, not dominated by one field or the other (though of course some individual laboratories and research centres are), but drawing on what Compton and Bunker (1939) would call the convergence of the disciplines in order to take a new perspective on biology. A perspective, that is, which views biological material as engineerable, and biological organisms as ready targets for synthesis.

[183] Such as Farnesene, a renewable 15-carbon, long-chain, branched, unsaturated hydrocarbon. Amyris intend to use this oil to produce fuels, as well as cosmetic oil, lubricants, and high-performance rubber such as is used in the tyre industry (Gardner and Hawkins 2013).

The newly emerging disciplines at this crossroads are collaborative by nature, drawing participants from across the life sciences and various branches of engineering. As was noted in chapter four, within synthetic biology these engineers are not playing a supportive role, but rather are full collaborators. They are not only designing the organisms and the experiments, but at times are also working in the laboratories to 'build' them. Indeed, while the centre I studied contained more biologists than engineers, some such as Endy (2008), and Tucker and Zilinskas (2006), go so far as to contend that the future of synthetic biology will ultimately be as an engineering discipline. A discipline, they predict, which will be dominated by engineers. Engineers who will require no background in biology, nor experience with basic biological research at all (Endy 2008). It is, therefore, these shifts within biology that led me to question whether we are seeing the beginnings of a new conception of life. Is life as information being replaced by the notion that life is made up of engineerable material, despite the obstacles to enacting this vision? Indeed Endy, one of the guiding lights of synthetic biology, glossed over these obstacles when he wrote that "the stuff of life" was essentially "reproducing machines" which can be designed and built (Endy 2008: 343).

As discussed in previous chapters, any such shift towards the notion of life as engineerable material is occurring in spite of difficulties with actually engineering life as the prevailing rhetoric suggests. This is in part attributable to the scientific and technological advances (such as those exhibited in the creation of syn3.0) which are fuelling the belief that the engineering approach will prove to be revolutionary for biology. However scientific and technological shifts are arguably not enough in themselves to bring about a new conceptual model for life.

Ortony (1993), for example, argues that it would be a mistake to underestimate the capacity of discourse to shape the future of science. Metaphors, he stresses, are not merely linguistic tools, but rather they are necessary for our thinking, our acting, and our speaking. Keller also addresses the influence of language on people's thoughts and actions when she notes, in regards to scientists, "[b]y their words, their very landscapes of possibility are shaped" (2000: 139). Thus, just as the post-war drive towards information theory, and the introduction of a new language for biology, helped to usher in the notion of life as information; while new mechanical analogies, and the wider influence of a mechanistic worldview, boosted Descartes' case for life as mechanism; so too does the notion of life as engineerable material rely on discursive and cultural shifts to gain purchase.

Landscapes of possibility

Balmer and Herreman (2009) note that the dominant metaphor in biology has shifted since the end of the Human Genome Project, from the literary allegory of reading the book of life, to the computational metaphors (e.g. writing software for the cell) and engineering metaphors (e.g. designing and building life) used by synthetic biology. As Konopka asserts, "the machine metaphor is perhaps the most powerful conceptual tool of modern biology" (2002: 398). The development of such metaphors, and of the programmes of work these metaphors both describe and bring to life, would therefore seem to be linked to the engineering language that pervades biological discourse. As discussed in chapter four, words such as 'mechanism,' 'program,' 'design,' 'control,' 'feedback,' 'regulation,' 'switch,' 'input,' 'output,' and 'efficiency,' which Nicholson (2012) contends have their basis in the mechanistic conception of the organism, are now commonplace in biology once more. Playing, as they do, a central role in the description and conception of synthetic biology. Such shifts in the language of biology are arguably just an example of language evolving, a process that happens as much in science as it does elsewhere. However, according to Keller, this process is not only inevitable, it is essential to our understanding of the world. Indeed, she writes that "our understanding of the natural world could scarcely progress without such evolution" (Keller 2000: 144).

Drawing on Keller's work then, synthetic biology's use of such engineering terminology may well be shaping the perceived landscapes of possibility for the discipline and those working within it, as well as altering our understandings of the natural world. As was discussed in chapter four, synthetic biology has taken its engineering terminology, and the accompanying engineering approach that it suggests, to heart, and this is in turn shaping the way in which both the work of synthetic biologists, and the products of their work, are conceived. Take for example the following quotes from Drew Endy:

> "Most engineers have not looked at self-replicating machines before" (Endy quoted in Lentzos et al. 2008: 317).

> "The question arises, how do we design reproducing machines whose designs we can also understand? It's a new problem for most engineers, so figuring that one out is going to be pretty exciting" (Endy quoted in Lentzos et al. 2008: 317).

Here Endy does not refer to the products of synthetic biology as organisms, nor those looking at them as biologists, or even synthetic biologists, but rather he terms such products "*self-replicating machines*" and "*reproducing machines*," and those investigating and designing them, "*engineers*." Such language is powerful. As Rose and Miller assert, language can be seen as a kind of intellectual technology for rendering the world thinkable and practicable (P. Miller and Rose 1990; N. Rose and Miller 2010). Thus, the mechanical, practical, interventionist language synthetic biologists are embracing can be seen to be affecting the way they think about and act within the world. As Vincent writes, despite diversity in their engineering ideals and practices, "all synthetic biologists seem to share the conviction that designing or redesigning organisms is making the future" (2013: 26). Thus, through their speech acts, synthetic biologists are shaping "a specific vision of the future, as being in the hands of humans," (Vincent 2013: 26). Furthermore, they are following this conviction with action that is ultimately shaping reality.

Taking these insights from Keller, Vincent, and Miller and Rose then, we can perhaps think of synthetic biology's adoption of metaphors and terminology from various fields of engineering as not only an act of discipline building, as was be discussed in chapter four, but also as an influence on both the scope of the discipline, and on the synthetic biologists' understandings of the natural world. Yet it goes further than this, as the conviction that organisms can be treated as/like machines is arguably challenging the machine/organism divide in a whole new way, something that was discussed in chapter five. Yet to dig even deeper, the language shifts we are seeing within synthetic biology are arguably part of a wider cultural shift within our modern society generally. A shift, that is, towards the increasing technologisation of our lives and world,[184] which is influencing the emergence of the notion of life as engineerable material.

The 'technologisation' of life

Karen Kastenhofer (2007) maintains that the idea of life as technology is the result of an epistemic cultural shift within the life sciences towards a technoscientific paradigm. To this ends, she argues that shifts in the epistemic cultures of fields such as synthetic biology (as was discussed in chapter three) are part of a more general shift in the epistemic cultures of the life sciences. A shift that she maintains is being prompted by the continual convergence of the life sciences within the field of biotechnology.[185] Kastenhofer writes of this convergence that it "can be interpreted as cultural assimilation under a technoscientific paradigm" (2007: 367). Her subsequent definition of the technosciences[186] that result from such a cultural assimilation, does appear to describe synthetic biology rather well. She writes, "[t]he resulting technosciences favour specific epistemic characteristics, such as easily

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[184] See, for example, the current discussions regarding robots taking over more and more jobs and tasks (M. Ford 2015; McNeal 2015).

[185] The other examples mentioned by Kastenhofer (2007) are molecular biology, genetics, agricultural science, biomedicine, pharmacy, and biophysics.

[186] The term "technoscience" was first coined by Belgian philosopher Gilbert Hottois in the 1970s and was subsequently popularised by members of the science studies community including Bruno Latour (Hopkins 1928), and Donna Haraway, (1987). As Keller describes it, "[t]he term came to be employed to underscore the illusory character of the classical divides between representing and intervening, looking and touching, pure and applied science, and to do away with these divides. It was a manifestly polemical intervention, aimed at debunking the myth of pure science" (2009b: 293). However, she acknowledges that this is no longer the use to which the term is put. Writing that, "[t]hese days, however, we do not use the term 'technoscience' as a political/intellectual intervention, or as a statement of disillusionment, but simply as a characterization of the way things are" (2009b: 293).

controllable scientific objects, controlled experimental settings, high-throughput practices, a 'black boxing' of elements in the experimental system, and an orientation towards functionality and applicability rather than discovery or 'Verstehen' (comprehension)" (Kastenhofer 2007: 367).

If Kastenhofer is correct that there is a general shift within the life sciences towards the technoscientific (a view supported by Keller (2009b) and Clarke et al. (2010)), then this would help to explain the emergence in recent years of fields such as synthetic biology. Fields, that is, which lie at the crossroads of biology and engineering embracing elements from both disciplines. Such a paradigm shift would also support the notion, forwarded herein, that biology and engineering have reached a point of convergence. While also helping to explain why those from biology and engineering backgrounds are now interested in engaging with each other, where such engagement has been a stumbling point in the past. Yet, identifying an epistemic, or paradigmatic shift, as Kastenhofer attempts to do, is not akin to a claim that societal attitudes have uniformly shifted. Indeed, despite this current momentum towards the technologisation of life, and towards seeing life as engineerable material, there are those who have voiced concerns over such combinations of biology and engineering, who see the technologisation of life as potentially problematic.

Resistance to the technologisation of life

Despite writing extensively on the subject of biotechnology Bud, for example, argues that there is an inherent juxtaposition in the term "biotechnology". He notes that:

> "'Bio' suggests natural; it connotes all those living things whose lives, it often seems, would be better but for the human species. By contrast 'technology' evokes human control over nature. The combination of the two has often seemed deeply disturbing, even monstrous, as amalgams of people and machines have been described" (1993: 2-3).

Such concerns have indeed been raised in regards to synthetic biology by the ETC-group (ETC Group 2007, 2010), the media (Pauwels and Ifrim 2008; Pauwels et al. 2012), and the public (Pauwels 2009). All of whom have expressed discomfort with synthetic biology's engineering approach to life and have raised concerns that tinkering with life, and seeking to control it, is inherently dangerous and must be carefully managed. While, for others, their concern with the combination of biology and engineering revolves around its impact on biology as a fundamental science.

Foremost amongst such detractors of the technologisation of life is microbiologist Carl Woese. Woese argued that science is impelled by two main factors, technological advance and a guiding vision, and that it is key to the successful development of a science that these two are in balance. Woese contended that without the necessary technological advances, the science cannot move forward, but "without a guiding vision there is no road ahead; the science becomes an engineering discipline, concerned with temporal practical problems" (Woese 2004: 173). It is to this fate that Woese believes molecular biology has fallen. He writes that by the end of the twentieth century, molecular biology considered all of the big problems, such as the human genome, to be solved, and thus he argues that molecular biology lost its guiding vision. With the focus shifting from understanding to manipulating, Woese argues that molecular biology has become an engineering discipline obsessed with fundamental reductionism.

While Woese (2004) does not write on the subject of synthetic biology, a field that emerged towards the end of his life, given his aversion to biology becoming an engineering discipline, it is hard to imagine that he would support it. For although synthetic biology arguably has a guiding vision, in its desire to make biology easier to engineer, such a vision is scarcely in line with Woese's support for basic science and understanding. He wrote, for example, that "[a] society that permits biology to become an engineering discipline, that allows that science to slip into the role of changing the living world without trying to understand it, is a danger to itself" (Woese 2004: 173).

Woese claimed that the danger of such a reductionistic, interventionist approach is that, ‘it stripped the organism from its environment; separated it from its history, from the evolutionary flow; and shredded it into parts to the extent that a sense of the whole – the whole cell, the whole multicellular organism, the biosphere – was effectively gone” (Woese 2004: 179). Thus, despite what has appeared to be a slow but steady movement within biology towards a convergence with engineering, such an approach to the science, and its associated conception of life as engineerable material, has its detractors. Just as all previous conceptions of life have had.

However, what is different here is that, as Woese states, at this point of convergence, and under this conception of life, for the first time biology runs the risk of losing its status as a fundamental science by becoming little more than a tool for engineering. He writes, “[b]iology today is little more than an engineering discipline. Thus, biology is at the point where it must choose between two paths: either continue on its current track, in which case it will become mired in the present, in application, or break free of reductionist hegemony, reintegrate itself, and press forward once more as a fundamental science” (Woese 2004: 185).

If he were still alive, Woese would perhaps support the post-genomic shift of biology, given its drive to return attention to biology’s whole, and to engage with fundamental research. However, given that at least some synthetic biologists, including Endy (2008), Tucker and Zilinskas (2006), and indeed some members of the Centre (as discussed in chapter four), envision the future of synthetic biology as being dominated by engineers, it would seem that synthetic biology, and the other disciplines arising at the biology/engineering crossroads, are pressing on down the first of Woese’s paths. Whether these two trends in biology continue side-by-side, examples of the two paths Woese spoke of, or whether one falls out of favour as the other persists, remains to be seen.

Conclusion

What we can predict, however, is that the way we understand and 'do' biology is likely to continue evolving. Especially given Gayon's (2010) assertion that, despite millennia of investigation and examination, there remains no scientific consensus on the definition of biology's defining concept, 'life.' Yet, despite this lack of consensus, as each of the various dominant conceptions of life, detailed in this chapter, arose, they captured the imagination of those who study life and biology. Thus shaping not only the scientists' 'landscapes of possibility,' but also the direction and focus of the science of biology itself.

Each of these conceptions of life drew on those that came before, reframing past ideas and repurposing language, but still forming a trail of thought that spans back 2366 years to Aristotle's concept of life as animation. As I have highlighted in this chapter, throughout the twists and turns of this trail of thought, mechanism and the technologisation of life have slowly been growing more and more persistent, and burrowing deeper and deeper into our understandings of life. While this has been a slow process it has, as I have outlined above, arguably brought biology to a point of convergence with engineering. A point where ideas, language, and methods from engineering are shaping the way biology is spoken about, understood, and engaged with. A point where not only organisms, their tissues, their movements, their cells, and their DNA are understood mechanistically, but where it is believed that engineers can use this conception of life to build biological machines. Life, it is maintained, not only resembles engineerable material, it is engineerable material.

From this position, synthetic biology, with its heavily mechanistic reductionism, is clearly building on the work of modern biotechnology. Drawing on the biotechnological notion that biology is a manufacturing technology, synthetic biologists are addressing the perceived 'failure' of the human genome project to produce a digital parts list for an organism by attempting to design and build their own standardised, universal parts list.[187] A parts list that, some maintain, can then be used to construct organisms. Thus they are seeing life as the raw materials, like any other construction materials, for the development of engineering projects. Mechanism here is not just an explanatory or descriptive tool but rather; as the focus shifted from understanding to building, biology has, arguably, finally entered its long anticipated synthetic phase.

Furthermore, while synthetic biology, with its drive to design and build synthetic organisms, fits underneath the umbrella of biotechnology, it nevertheless bears a significant difference to the biotechnology that came before. This difference lies with the role of engineers. Engineers have, as I outline above, long played a part in modern biotechnology, however this has ordinarily been in a supportive role, designing and engineering the equipment and processes. In synthetic biology, as in other contemporary disciplines emerging at the crossroads of biology and engineering, the role of engineers is much more central, and the targets of their engineering concepts, methods, and approach are the organisms themselves. Indeed synthetic biology has embraced engineering so completely that it is conceived of by some as an engineering, rather than a biological, discipline.

This swing within the life sciences towards engineering has been termed a technoscientific shift by Kastenhofer (2007). A term she uses to encapsulate this epistemic shift in our interactions with, and interpretations of, life. This shift is, I contend, having a profound impact on our conception of life. As emerging hybrid disciplines such as synthetic biology, strive to apply their highly mechanistic version of reductionism to their encounters with biology, they are bringing into being a new conception of life, life as engineerable material. Consequently, and in conclusion, I would respond to Jacob's question of what analysis will next break down biology and reconstitute it in a new space, with the answer: engineering. We are, I believe, rightly or wrongly

[187] Most notably the iGEM Registry of Standard Biological Parts which currently contains over 20000 documented parts (iGEM).

seeing the beginnings of a new conception of life that fits into our increasingly technologised world. This conception is of life as engineerable material, and synthetic biology is its poster child.

Chapter Seven: Conclusion

As discussed in chapter four, the prevailing rhetoric surrounding the emerging discipline of synthetic biology frames it as an unproblematic hybrid endeavour, which draws on both engineering and biology but which is neither solely one nor the other. A biotechnological discipline, which is applying a rational engineering approach to biology in order to design and produce synthetic organisms that perform predetermined, desired functions as biological machines. Yet, underneath the gloss of synthetic biology, the so-called harbinger of the next industrial revolution, is a world brimming with stories, stories that are obscured by this oversimplified rhetoric. Within the newly established, dedicated, academic research centre where I undertook my research I encountered stories of conflict and compromise, confusion and classification, constraint and collaboration, all encapsulated within synthetic biology's attempt to control life at a molecular level. Thus in attempting to lift the lid on synthetic biology, to see how accurately the prevailing rhetoric played out in practice, I discovered a far messier and more interesting world. The stories of this world, which weave their way through this thesis, thus paint a much fuller picture of the developing discipline than the rhetoric alone.

From these many stories I have teased out two overarching tales. The first is the story of the formation of synthetic biology as it played out in a newly established, dedicated, academic research centre. I have offered here an ethnographic account of the hard work, conflict, collaboration, and compromise that such an attempt at disciplinary formation requires. A case study that ultimately explores the features of the emerging discipline that go unrecognised by a prevailing rhetoric that conceals, rather than illuminates, the reality of the discipline's day-to-day work. Whereas the second overarching story within this thesis, explores the work to bring to fruition synthetic biology's goal of applying a stringently reductionistic and mechanistic approach to biology, and the history behind this approach. I have focused not on whether such reductionism is appropriate but rather on how the practical and conceptual challenges its application entails are navigated by the synthetic biologists at the Centre, and ultimately how synthetic biology's embrace of engineering and reductionism is shaping the way biology is thought about and 'done.'[188]

Disciplinary formation

The story of the emergence of synthetic biology, as it played out within the Centre, is woven through chapters two, three, and four. The Centre itself, that gleaming, glass-walled space spread over two levels of the Engineering School of a prestigious UK university, and filled with people and equipment, is evidence in and of itself of the funding being poured into, and the infrastructure being assembled in the name of, synthetic biology. As Leonelli and Ankeny (2015) attest, such infrastructural features and resources are key to the creation of resilient scientific communities. Collaborative communities that must move beyond short-term projects in order to establish themselves as disciplines in their own right. Leonelli and Ankeny (2015) term the distinctive and shared ensemble of elements required for such an establishment a 'repertoire,' while Fujimura (1987) refers to the alignment of such elements as the formation of 'doability.' Both, as I argue in chapter four, can be seen as core elements in the formation of a new epistemic culture, and thus a new discipline. However, while the Centre clearly displayed the necessary physical and material components of a repertoire, it was, I discovered, the social, conceptual, and practical elements that required greater effort to instigate.

Indeed, the synthetic biologists at the Centre had the disciplinary name, the laboratories, the people, the equipment, the high profile cross-research council funding, the conferences to attend, and the journals to publish in. All factors at the experiment, laboratory, and social levels that, according to Fujimura (1987), need to be aligned in order to establish a scientific problem

[188] Given that this case study explores one site, located in one country, during one year, the findings I present here may not ring true for other sites, countries, and times. Nevertheless, my findings were supported by my many observations of other synthetic biology settings and meetings, in the U.K., the U.S. and Japan.

as doable. However, instituting the practical and conceptual norms to aid collaboration and cooperation between synthetic biologists hailing from biology and those from engineering was far from easy. Yet the common call for such norms from both Leonelli and Ankeny (2015), and Fujimura (1987), suggests they play a key part in the establishment of a resilient research community which is focused on a doable problem. As such, chapters three and four explored the challenges of establishing such practical and conceptual norms within the emerging hybrid discipline of synthetic biology.

Clearly, despite the rhetoric about synthetic biology being a hybrid discipline, achieving the hybridisation of ideas from biology and engineering, and the collaboration between engineers and biologists that this requires, is a challenging task. Chapter three explicitly explored this challenge within the Centre, arguing that the difficulties the synthetic biologists face in bringing the two 'sides' of the discipline together stem from the epistemic cultural differences between biology and engineering. Indeed, through ethnographic observations, and both informal and formal interviews, I became aware of significant disparities between those who hailed from biology and those from engineering, in terms of their language use, knowledge base, methods, research questions, research objects, and general approach to research and data. These differences, it became apparent, are the cause of frustrations and tensions, misunderstandings and miscommunications, and are, I maintain, hurdles that need to be overcome in order to establish a clear, coherent, yet hybrid, epistemic culture for the developing discipline.

I argued in chapter three that negotiating these hurdles requires that the synthetic biologists bridge the epistemic cultural divide between the two 'sides' of the discipline, and throughout my fieldwork I observed clear attempts to do so. Driven by a desire and determination to 'make synthetic biology work' those at the Centre were largely working hard to bridge this epistemic gap, and these efforts form part of the story of the unsung struggles to bring the discipline of synthetic biology to life. Efforts, that is, which are glossed over by the prevailing rhetoric that presents it as easy, and straightforward. These efforts included the adoption of a shared language (even if it did not sit well with everyone), the sharing of research objects (though they interacted with them in very different forms, i.e. as colonies of organisms to experiment with or as numbers to feed into mathematical equations), and the formation of hybrid research projects.

Through my fieldwork I encountered two distinct strategies for drawing on both sides of the discipline's knowledge base, research questions, and methods, in order to develop such hybrid projects. These two strategies, namely the formation of close, collaborative working relationships, and the attempts by primarily doctoral students to become interdisciplinary individuals were, I contend, playing a role in the establishment of synthetic biology as a coherent discipline with a coherent, and distinct approach to engaging with biology. Within both strategies, the synthetic biologists were attempting to move beyond the limits of their previous training (either by working closely with someone with a different knowledge and skill base, or by acquiring new knowledge and skills themselves), and in this way they were striving to achieve the generation of new science, and new scientific knowledge, which is central to the establishment of a new discipline. Yet despite the commitment to such a hybrid approach, I would argue that synthetic biology has not yet achieved the cohesion of an established discipline. That is, although chapter three tells the story of a discipline in the process of hybridising, of merging, or fusing, I argue that, due to the persistent, epistemic cultural differences within the discipline, it has not yet achieved this ends.

The state of synthetic biology's hybridity, as I discuss in chapter three, brings to mind cell fusion. During the formation of new disciplines like synthetic biology there are, I contend, intermediate states between the component parts being separate entities and their merging to become a single hybrid entity. Furthermore, I contend that an interdiscipline like the reproductive sciences, which involves distinctive subworlds (A. Clarke 1998), is quite different to one like physics, which has coalesced to such a degree that it has formed a cohesive singular discipline (albeit with internal specialities). Both kinds of interdisciplinary research community are formed through collaboration but I contend that, as they draw on different kinds of collaboration, we can draw on different intercellular interaction analogies to explore them.

In the case of interdisciplinary collaborations such as the reproductive sciences, where the aim is to create a research community with shared objects, but different disciplinary approaches to engaging with them, I draw on the analogy of intercellular interactions within the immune system. The immune system involves different types of cells communicating, interacting, and 'cooperating' on a common goal, but remaining distinct and independent throughout. Meanwhile interdisciplinary endeavours such as physics, neuroscience, and synthetic biology are, I contend, better represented by the analogy of cell fusion. However, where physics has achieved the merging and hybridising of its constituent nuclei, or epistemic cultures (mathematics and natural philosophy), in order to become a cohesive interdiscipline, synthetic biology has not. Rather, while it has a shared disciplinary boundary, analogous to a cell wall, and is working towards having shared universal disciplinary components (language, research objects, questions, methods etc.), it does not yet have a unified epistemic cultural 'nucleus.' As such, although synthetic biology is working hard to overcome its internal epistemic cultural division, given the persistent talk of 'us' and 'them' and the 'wet-lab'/biology, and 'dry-lab'/modelling 'sides' of the discipline, it has not yet achieved this. I would therefore contend that as a discipline synthetic biology is yet to undergo the equivalent of nuclear fusion. It is in a grey zone between being two distinct, but interacting, disciplines, and being a cohesive, hybrid discipline, with a hybridised epistemic culture. This, I maintain, is a boundary spanning zone which, as I shall discuss below, parallels that of the products they make.

Nevertheless, the challenges of negotiating this disciplinary boundary spanning zone, by bridging the epistemic cultural divide between the discipline's two sides, is not the only challenge that synthetic biology faces as it strives to establish itself as a coherent discipline working on a doable problem. Rather, as stated above, the Centre's inhabitants face both conflicts and compromises as they strive to establish the discipline's practical and conceptual norms. As discussed in chapter four, synthetic biology not only strives to hybridise the disciplines of engineering and biology, but does so with the expressed goal of engineering biology (Endy 2005). However, this application of an engineering approach to biology, like the hybridisation of the disciplines, is a lot easier said than done. As addressed in chapter four, underpinning synthetic biology's engineering approach is an emphasis on synthesis over analysis. A prioritisation that has become a key conceptual element of synthetic biology's developing repertoire.

Such a prioritisation of synthesis, and adherence to the language and modes of working of engineering is, for synthetic biology, not only an act of repertoire building but of establishing disciplinary borders. To these ends, I found that those within the Centre drew heavily on an idealised version of what engineering is, in order to demarcate the field of synthetic biology from biology and align it with engineering. By appropriating engineering's supposedly efficient, rigorous, and logical approach, the Centre framed synthetic biology as distinct from 'traditional' biology. Presenting it as a discipline with a revolutionary way of interacting with, and ultimately controlling, biology and life. Nevertheless, while this appropriation was shaping the emerging discipline's conceptual and practical norms, the engineering practices, which were professed to make up these new norms, were all a lot harder to apply in reality.

Standardisation, the abstraction hierarchy, the design cycle, and using mathematical modelling for design and control (rather than representation), are all core elements of the Centre's engineering approach. Yet these engineering-derived concepts and processes all currently require significant modifications, or omissions, in order to be applicable to biology. This difficulty is, in large part, due to our dearth of understanding regarding biology, as recently demonstrated by syn3.0.[189] This degree of ignorance makes the goal of fully standardising and characterising bio-parts problematic, to say

[189] The minimal cell with a genome of 473 genes, 149 of which are not understood (Clyde A. Hutchison et al. 2016).

the least. Furthermore, this situation makes the application of engineering concepts and practices, designed as they are for the manipulation and control of standardised and well-characterised materials, challenging. Thus I argued in chapter four that, although the prevailing rhetoric surrounding synthetic biology suggests that applying an engineering approach to biology is straightforward, in the Centre at least, this application required a fair amount of kludging.

No single element of the engineering approach was applied seamlessly to biology within the Centre; rather, the synthetic biologists I spoke with did the best they could with approximations and modifications. Indeed, despite the gulf between the reality of the engineering content of their work and the prevailing rhetoric, they seemed to be making their kludged version of the engineering approach work. The language, research questions, experiments, models, data gathering, and working relationships, of those at the Centre were all being altered by this kludged version of an engineering approach. Thus, despite its challenges and limited applicability, those at the Centre were ultimately using it to shape the repertoire, and the practical and conceptual norms, for the synthetic biology community. Moreover, given that the research problem they are seeking to render doable is the application of an engineering approach to biology, through standardising the Centre's approach to their work using this assortment of kludged concepts and practices from engineering they are also, ultimately, increasing the doability of this research agenda. However, it is important to note that this is not the same as saying that biology will prove to be engineerable in the way the rhetoric they adhere to professes it will. Indeed, whether or not synthetic biology will ever manage to design and build organisms from the 'bottom up' using solely standardised, well-characterised bioparts, is something even synthetic biologists are uncertain of, optimistic about certainly, but uncertain of nonetheless.

As such I would contend that the story of synthetic biology' emergence, as it played out in the Centre during my fieldwork, was one of an interdiscipline in the process of merging its constituent parts. This is a challenging process, which may, or may not, yield a new cohesive hybrid discipline with characteristics of both biology and engineering. Cell fusion, after all, has a high failure rate. However, at least for now, the hybridisation I observed was incomplete, and the internal struggles to create the conceptual and practical norms for the developing hybrid discipline were very real. These challenges were being tackled using the application of an engineering approach to just about everything – the language, the experimental questions, the data, and the research strategies. However the engineering approach being applied was not the hallowed, pure, idealised approach of engineering that synthetic biology ostensibly embraces. In practice, this was a kludged engineering approach, an improvised, inelegant engineering that, despite its cobbled together nature, was nevertheless shaping the discipline, and its emerging, hybrid, epistemic culture.

Reductionism and complexity

The second story that winds through this thesis also takes as its starting point the discipline's claims regarding applying an engineering approach to biology. However, where the story of synthetic biology's emergence examines the practical aspects of such an engineering approach, and the ways it is negotiated and enacted across an epistemic cultural divide, this second story explores the conceptual challenges of applying the approach's explicit reductionism and mechanism at the biological coalface. The engineering approach itself, its goals, concepts, and language are replete with reductionism and mechanism. Yet, as discussed above, there is still so much that is unknown about biology, and this realm of the unknown is a hindrance to the application of reductionism.

As discussed in chapter one, Francis Crick (1966) argued that the way to refute vitalism, the sworn enemy of reductionism, would be to create a living organism synthetically. However, he contended that understanding the cell was a more important goal. Venter claimed to have achieved this first goal with Synthia, declaring 'her' to be a synthetic organism, however with his subsequent 'synthetic' organism syn3.0 he acknowledged that, as a third of the organism's genome defied understanding, his team had not yet achieved this second, more fundamental, goal. This degree of uncertainty undermines the application of reductionism, and its drive to explain life completely in physico-chemical terms, and therefore also the ability to create synthetic organisms from standardised, well-characterised parts (though this has never been Venter's approach to synthetic biology[190]). Indeed, as Jim Collins, one of the early proponents of synthetic biology's reductionistic approach to biology, acknowledges, "synthetic biology projects are frequently thwarted when engineering runs up against the complexity of biology" (2014: 155). Leaving synthetic biologists in a situation whereby they "do not yet know enough biology to make synthetic biology a predictable engineering discipline" (2014: 155).

Thus, there remains a clear gap between the reality and the rhetoric of applying a reductionistic, mechanistic, engineering approach to biology. Within the Centre I encountered this gap in both the efforts to hybridise the discipline, by bringing the engineers and biologists together, as discussed above, and within the struggles those at the Centre faced in trying to conceptually and practically adhere to the reductionism of the engineering approach. Foremost amongst the causes of this latter challenge appeared to be the realm of the unknown in biology, which is often alluded to using the term 'complexity.' While this may seem to be a major hindrance to their adherence to a conceptual model of life drawn from engineering, according to Paul Feyerabend,[191] such an incompatibility between a new conceptual system, and current, observable, 'reality' is not uncommon. Indeed Feyerabend argues that, "hardly any theory is consistent with the facts" (1993: 50) and thus the test of a new conceptual system's value comes only after we "*wait* and . . . *ignore* large masses of critical observations and measurements" (1993: 113).

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[190] As discussed in chapter one, Venter adheres to the genomes approach rather than the parts-devices-systems approach that prioritises standardisation, characterisation, and abstraction.

[191] It should however be noted that Feyerabend's work concerned the experimental sciences rather than those, like synthetic biology, which seek to build artefacts.

Drawing on the work of Feyerabend, Dan-Cohen (2016) argues that in the case of synthetic biology, biology's complexity has been ignored, and ignored intentionally. Indeed she writes that within synthetic biology, those hailing from engineering have made use of "selective ignorance of the biological substrate . . . in order to evacuate biology of some naturalized content and recolonize it with new conceptual frameworks and knowledge practices" drawn from engineering (Dan-Cohen 2016: 10). This embrace of ignorance regarding biology's complexity, which initially drove the discipline forward, was also clear in Alan's[192] belief that "*we don't need to know how it works, we just need to know the inputs and outputs*." Thus, despite the increasing acknowledgment within the synthetic biology community that complexity needs to be addressed (Dan-Cohen 2016), within the Centre I observed an oscillation between this standpoint and that expressed by Alan. A position characterised by a continued embrace of engineering's reductionistic approach, and a sustained belief that engineering's simplicity will ultimately overcome biology's complexity. This kind of optimism, Keller (2009a) notes, is underpinned by our growing understanding of self-organised complexity. A situation that, she argues, is leading some to hope that a full account of life, and its complexities, may finally be within grasp.

Nevertheless, the persistence of the synthetic biologists' hope and belief in this promise of synthetic biology, even in the face of the significant practical and epistemic difficulties they encountered, brings to mind the literature on the sociology of expectations. Yet, where this literature often casts hope and hype as hyperbolic and performative tools used in the public and academic spheres to set expectations and priorities, and attract investment in order to manifest a particular future (Borup et al. 2006; Kitzinger 2008; Van Lente 2012), here we see hope in action as a motivating and formative feature of an emerging discipline at the personal level. A source, that is, of motivation for the practitioners themselves, which must be maintained in order for them to keep pushing forward in the face of great obstacles.

[192] One of the Centre's directors.

Indeed, the synthetic biologists I encountered were still, largely, hoping to use their version of an engineering approach to design and build novel biological entities that will produce, or act as, industrialisable products, in spite of the degree of uncertainty and unexplained complexity in their dealings with biology. As discussed in chapter five, this conundrum ultimately raises questions about which category these 'products' might ultimately fit into – machines, organisms, or a third, as yet undefined, boundary spanning or hybrid category. Given the discipline's drive to align itself with engineering, to embrace reductionism, and to view and treat life as engineerable material, I would not have been surprised to find that the members of the Centre saw the 'products' of their work as machines, or at least as being indistinguishable from machines. However, as explored in chapter five, I found the members of the Centre to be genuinely conflicted about how to categorise what they were producing.

Despite synthetic biology ostensibly being the current pinnacle of reductionism and mechanism in biology, those trying to enact its reductionistic engineering approach within biology were struggling to do so. There was a sense that many thought they 'should' see their 'products' as machines, but they found themselves reluctant to categorise them as such. This reluctance was sometimes attributed to the 'products'' lack of certain characteristics, characteristics that would distinguish them as machines. These features were, namely, being well understood, controllable, stable, reliable, and designed and built from 'scratch,' all of which would require, as a basis, the full understanding of the underlying biology.

Yet, there were also arguments made that the discipline's 'products' do not, currently, fit into the category of 'machine' due to characteristics they do possess, characteristics that demarcate them as organisms, as being alive. These distinguishing characteristics, or as Keller (2002) would have it, honoured differences in the human category of life, were the ability to reproduce, self-repair, evolve, and exercise free will, among other potentialities. While some within the Centre maintained that it was only a matter of time before such characteristics of life could be controlled, and those of machines could be engineered into the discipline's 'products,' others upheld a belief in the existence of a fundamental difference between animate and inanimate entities that wasn't so easy to overcome.

Thus even within synthetic biology there was some resistance to excessive mechanism and reductionism, and the understanding of life such an approach promotes. This is despite the discipline arguably being the epitome of the reductionist mechanisation of life, where mechanism underpins their very interactions with biology. While this resistance was explained in terms of biology's complexity rather than any vital principle, some nevertheless maintained that life was '*different*,' biology was '*biology*,' and organisms were '*not machines*.' Yet, such assertions, and the belief that biology is inherently different from engineering, and thus resistant to engineering's methods and approaches, were often accompanied by claims that taking an engineering approach to biology was appropriate and would likely prove successful.

While ostensibly conflicting, I would argue that such mixed responses are an unsurprising result of the hybrid discipline they align themselves with. Given that, in spite of their embrace of both mechanism as a way of interacting with biology, and of the methods and discourse of an idealised version of engineering, many of the members of the Centre still hailed from the life sciences. These synthetic biologists had spent many years learning about, and encountering, all that we do not yet completely understand about life, and all the ways in which it is remarkable. It was then, I would contend, hard to set aside biology's tendency to, as Malcolm puts it in chapter four, "*deconstruct things*" in order to generate knowledge, in order to focus only on engineering's affinity for constructing things in order to generate industrialisable products.

Furthermore, I would contend that biological organisms are not only perceived as being different from entities engineers have traditionally worked on and with, but that they fundamentally are different. Typically engineers take simple, standardised, well-characterised parts and put them together to build a complex construct. Whereas in synthetic biology they are faced with the arguably more challenging task of starting with a complex construct (the organism), one that, despite the reductionistic rhetoric, is not completely understood. They are then trying to deduce the function of its constituent parts, in order to standardise and characterise them, so that they can use these parts to build other complex, and controlled, constructs. Consequently, while many of those at the Centre find themselves striving forward with the engineering approach, they do so while also maintaining an awareness of the biological limitations. The practical and conceptual hurdles, complexities, and knowledge gaps that is, which would need to be negotiated in order to truly succeed in applying the reductionistic, mechanistic approach required to truly equate biological matter with other engineering materials. I contend, therefore, that this familiarity with both sides of their discipline, the entities each side deals with (organisms in the case of biology and machines in the case of engineering), and the complexities of applying reductionism to biology, results in the hybrid category many at the Centre chose to assign their 'products' to.

Indeed, following some deliberation, most of the members of the Centre settled, often uncertainly, for assigning the discipline's 'products' to a liminal zone, rather than to either the category of machines or organisms. A blurry, grey, boundary spanning, hybrid category between machines and organisms, where the 'products' are not fully one or the other, but rather are, as Max would have it, "*machiney-something elseys*." This uncertainty, displayed by all but one of the members of the Centre, in regards to such classification is, as I argued in chapter five, indicative of the complexity that lies within such a task. A complexity made all the more so by the unpredictability, and uncontrollability, of the biological organisms they work with, and thus the difficulty of rigidly applying the hallowed reductionistic, mechanistic approach.

Furthermore, the struggles those at the Centre faced in categorising the entities they produced appears to highlight a parallel situation between the discipline and its products. Given that, in both cases there is uncertainty about classification. Much as synthetic biology currently fits within a blurry, boundary spanning, interdisciplinary space, so too do its products belong in a grey area, at least in the minds of those who create them. As such, I would contend that in their uncertainty, and in their grapplings with reductionism, the synthetic biologists at the Centre are crafting a boundary spanning conceptual category, for the boundary spanning products, of their boundary spanning discipline. A category that allows their products to concurrently possess characteristics of both organisms and machines without the need to definitively, and permanently, claim them as one or the other. Thus much like light can simultaneously be both a wave and a particle, perhaps synthetic biology can be both biology and engineering and its products, both machine and organism.

Such a hybrid category would not only challenge the long held machine/organism divide, but would also challenge our concepts and evaluations of both life and machines. While many of those at the Centre expressed a reticence regarding making grand claims for synthetic biology, their emerging discipline is undoubtedly making waves. While these are currently small fluctuations on the surface of the life sciences they may, with time, grow larger and ripple out further, potentially shifting our conception of life, our understanding of biology, and our attitude towards the biological products of biotechnical research and development. Yet these small waves may also dissipate, fail to gain momentum, and ultimately blend back into the surface of the life sciences. A surface that will instead rise, fall, and move with some other conceptual, epistemic, and practical shift. So, perhaps unsatisfyingly, nothing about the future of synthetic biology is certain. As discussed in chapter six, the study of life has shifted conceptually and practically time and again. The conceptions of life distinguished by Canguilhem (2000), those of life as animation, life as mechanism, life as organisation, and life as information, may not have been the only ways in which life has been understood in the last 2500 years. But they are the ones that have gained traction and sufficient following to significantly shape the scientific and societal imagination. Consequently, while I would suggest that synthetic biology and its engineering approach have the potential to shape the scientific and societal imagination, it remains to be seen whether they gain the required traction to do so.

Life as engineerable material

As addressed in chapter six, the conceptions of life listed above have, through their discursive and conceptual practices, crafted what Keller (2000) refers to as the scientists' 'landscapes of possibility.' Which have in turn shaped their thoughts and actions and therefore the direction and focus of the science itself. Yet despite significant conceptual differences between these shifts in the landscapes of possibility for the life sciences, I suggest that there has been slow but steady movement towards a point of convergence between biology and engineering since Aristotle's time. This has taken the form of an increasing reliance on mechanism as an explanatory tool for understanding the form and function of increasingly minute components of living organisms, and thus the slow creep of reductionism deeper, and deeper, into our conceptions of life. This tightening embrace of mechanism and reductionism is clear in the increasingly interventionist approach to biology that has been prominent since the late nineteenth century, as well as in the birth of modern biotechnology in the first half of the twentieth century.

These two developments have, I argue, been instrumental in biology's increasing focus on synthesis, rather than description or analysis, as a way of interacting with 'life.' Thus, with this in mind, chapter six traced the roots of synthetic biology's reductionism by mapping the conceptual and practical shifts that have brought us to this point of convergence between biology and engineering. A meeting of the disciplines that is not only evident in the growing number of disciplines forming at their intersection but also, as Kastenhofer (2007) claims, a more general epistemic shift in the life sciences towards a technoscientific paradigm.

Synthetic biology epitomises this incursion of technology, and indeed engineering, into the life sciences, a shift that is arguably mirrored by an increasing trend towards the technologisation of our lives and our interactions with the world around us. Thus, despite the conceptual and practical difficulties discussed above, within the social and scientific context of this technoscientific shift, synthetic biology continues to strive forward with its brand of reductionism. Advancing its simplification of life with developments like syn3.0 (Clyde A. Hutchison et al. 2016), and spreading its engineering approach further into the life sciences. This desire for expansion is perhaps most striking in the recent proposals for a human synthetic biology consortium (Callaway 2016). Under the name of the 'Human Genome Project – Write,' this public-private initiative is coalescing around the aim of synthesising a human genome from scratch, much as Venter's team have synthesised small bacterial genomes. This is being proposed with the aim of developing technologies that would reduce the cost of engineering and testing large genomes in cell lines, while also addressing issues of human health[193] (Boeke et al. 2016).

Although some within the synthetic biology community are calling into question the justification for this project (Callaway 2016), the momentum it is gaining further suggests that Kastenhofer's (2007) claim, regarding a shift in our interaction and interpretation of life, has weight. Indeed, in chapter six I take Kastenhofer's argument a step further, arguing that such an embrace of the technoscientific within the life sciences is resulting in a conceptual shift in the way life is being understood, studied, engaged with, and spoken about. A shift, I maintain, towards seeing, and treating, life as engineerable material. This conceptual change is, as I see it, the overarching story of synthetic biology. The story of an endeavour, among other parallel endeavours, to control life at the molecular level, which is gaining traction at this point in history in a way that previous attempts at creating a 'synthetic biology' did not.

While the current attempts to embrace an engineering approach to studying and interacting with biology, as synthetic biology does, may

[193] Human health challenges which have been highlighted as potential targets for the project include growing transplantable organs, engineering immunity to viruses into cell lines, and engineering cancer resistance into therapeutic cell lines (Boeke et al. 2016).

ultimately fail to shape biology's landscapes of possibility, such an approach does, at least at this point in time, appear to hold the potential to make such influential waves within the life sciences. As discussed previously, with its reliance on tools, concepts, methods, and participants drawn from both biology and engineering, synthetic biology is a discipline emerging at the crossroads of the two disciplines. A point of convergence between engineering and biology, the likes of which Compton and Bunker (1939) argued is instrumental in intellectual advances. Furthermore, the engineering discourse, and the machine metaphor that synthetic biology embraces, have been described as "the most powerful conceptual tool of modern biology" (Konopka 2002: 398). As such, and as the reaction to Craig Venter's 'Synthia' showed, the engineering approach[194] embraced by synthetic biology is clearly capturing the collective consciousness.

With its determination to design, control, and ultimately engineer life to behave in certain desired and determined ways, synthetic biology is taking the technologisation of life to a new level. Mechanism is no longer just a way of understanding life, through analogy, but rather of interacting with life, "a veritable methodology with which to construct complex biological systems from first principles" (de Lorenzo and Danchin 2008: 822). Furthermore, such work is not only being done in the name of engineering, but by engineers themselves. Despite the uncertainty of synthetic biology's future, and the resistance expressed by some to its approach, I ultimately argue in chapter six that, like the growing number of other disciplines emerging at the intersection of biology and engineering, synthetic biology is promoting a new conception of life, that of life as engineerable material.

Given the ripples the discipline is making with this new conception of life, with its bridging of engineering and biology's epistemic cultural divide, with integrating an engineering approach into biology, albeit a kludged one, and with potentially necessitating the creation of a boundary spanning category

[194] In all its manifestations, i.e. the parts and pathways approaches, the genomes approach, and the systems approach discussed in chapter one.

for its ‘products,’ synthetic biology certainly appears to be forging a new way of doing, thinking, and speaking about biology. This may all come to nothing, but we may also look back at the early twenty-first century as the point where biology and engineering converged, a point after which our understanding of life was never the same again.

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