The London School of Economics and Political Science

Going Synthetic: how scientists and engineers imagine and build a new biology

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A thesis submitted to the Department of Sociology of the London School of Economics and Political Science for the degree of Doctor of Philosophy, London, July 2011.

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).

Caitlin Cockerton

Abstract

Synthetic biology practitioners look through an engineer's lens at the incredibly complex, sensitive and seemingly endless resource of living reproductive material and contemplate turning biology into a substrate – composed of modular, well-characterised parts – that can be used to design and build new functional devices and systems. It is often explained that this vision for engineering biology may deliver future forms of efficient drug production, renewable sources of biofuel, methods to sense and remediate toxins and numerous other applications. Yet, synthetic biology remains a field in its infancy, facing a barrage of interconnected challenges across technical, social, ethical, legal and political realms. This multifaceted dynamic makes it a timely and important locus for socio-philosophical investigation.

This thesis provides a highly empirical ethnographic account of two research groups as they were challenged to design and build a microbiological machine for the International Genetically Engineered Machine competition (iGEM) in 2009. The work examines forms of knowledge and material production in synthetic biology and, in focusing on iGEM, argues that this field is not only a feat of technical engineering, but also one of social engineering as it educates and indoctrinates a next generation of researchers through this unique contest. In this narrative, one discovers a microsocial sphere in which new ideas and biological entities at the intersection of natural and synthetic kingdoms of life are being constructed. Forms of teaching, tools, practices and processes that make imagining, designing and building new living systems possible are illustrated. The reader is also introduced to some international stakeholders and dynamics at play. With gathering media interest, attention from art and design perspectives, as well as publications across social, philosophical, political and legal studies of this 'new' biotechnology, there is a great need for the kind of detailed, insider view that this thesis provides – it contributes to an informed space through which constructive questions may be asked as the debate around engineering synthetic life continues to unfold. As such, this work helps to enable a reflection on the kinds of intervention possible in the process of dreaming up ideas of potential future living machines. Involved collaborators, as well as the resistance of life itself, will ultimately govern the limits of synthetic biology.

Acknowledgments

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To the many people in the synthetic biology community whom I was fortunate enough to work with – particularly those at the University of Cambridge and Imperial College London (you know who you are): THANK YOU. I have learned a tremendous amount from you and this work would not be possible without you integrating me into the fascinating worlds of your ideas and practices. I'd like to express my gratitude for the time and insights I've received from Drew Endy, Christina Smolke, Randy Rettberg, Tom Knight, Piers Millet, members of the DIYbio community as well as a particular student of Pamela Silver's laboratory. A huge thanks is owed too to Daisy Ginsberg, James King and Fiona Raby for opening my eyes to imaginative and compelling frames of thought and production in the field of design interactions.

Finally, thank you to my family and friends. These last three years have seen me through significant challenges and your unwavering support could not be more appreciated.

This work is dedicated to my mother Lynne.

Contents

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Main characters

(i) University of Cambridge affiliates

Pseudonym	**Brief description**
Samuel	iGEM advisor (top-tier)
Geoffrey	iGEM advisor (top-tier)
Frederick	iGEM advisor (top-tier)
Andy	iGEM advisor; PhD student in synthetic biology; previously employed as iGEM Ambassador at MIT iGEM Head Quarters; previous iGEM team member (2005); engineering and biology disciplinary background
Douglas	iGEM advisor; microbial molecular biologist; laboratory manager and teaching technician
Emma	Biological sciences background; iGEM team member
Derek	Biological sciences background; iGEM team member
Eleonore	Biological sciences background; iGEM team member; blogs about life as a 'lab rat'
Senni	Biological sciences; iGEM team member
Chelsea	Physics background; iGEM team member
Alex	Engineering background; iGEM team member
Tobey	Engineering background; iGEM team member
Daisy Ginsberg (real name used, with permission)	Designer, artist and researcher interested in exploring future implications of emerging science, technologies and services (http://www.daisyginsberg.com/)
James King (real name used, with permission)	Speculative designer interested in how design applications for emerging biotechnologies can be used to explore their social and aesthetic implications (http://www.james-king.net/)

(ii) Imperial College London affiliates[1]

Pseudonym	**Brief description**
Roger	iGEM advisor (top-tier)
Bernard	iGEM advisor (top-tier)
John	iGEM advisor
Pierre	iGEM advisor
Max	iGEM advisor; PhD student in synthetic biology; previous iGEM team member (2007 and 2008)
Olivia	iGEM advisor
Zach	Biological sciences background; iGEM team member
Felicity	Biological sciences background; iGEM team member
Andrew	Biological sciences background; iGEM team member
Kajan	Biochemistry background; iGEM team member
Sita	Bioengineering background; iGEM team member
Nisha	Bioengineering background; iGEM team member
Soo	Engineering background; iGEM team member
Matt	Bioengineering background; iGEM team member

[1] One advisor did not play a much of a role in the team and declined interview at the end of my research period. I had very little interaction with him and he is not included in the character list.

Key terms and abbreviations

BBF: "The BioBricks Foundation (BBF) is a not-for-profit organization founded by engineers and scientists from MIT, Harvard, and UCSF with significant experience in both non-profit and commercial biotechnology research. BBF encourages the development and responsible use of technologies based on BioBrick™ standard DNA parts that encode basic biological functions...."[2]

BioBrick™[3]: A BioBrick™ standard biological part is a standard biological part that meets the technical and legal standards set forth by the BioBricks Foundation (BBF). Each distinct BioBrick™ standard biological part is a nucleic acid-encoded molecular biological function (e.g., turn on/off gene expression), along with the associated information defining and describing the part.[4]
BioBricks™ come in various forms[5]:

- At the most basic level, they are "parts" (e.g. RNA, DNA, regulatory region, protein coding region);
- A level of sophistication higher, they are "devices" (e.g. with functions such as signaling or inversion);
- And, one step higher, they are "systems" (e.g. that measure).
- Other kinds of parts include chassis, vectors and flags.

BioBricks (in ideal form) have standard methods of assembly and characterisation.[6]

BIOFAB: "The BIOFAB: International Open Facility Advancing Biotechnology (BIOFAB) was founded in December 2009 as the world's first biological design-build facility. This professionally staffed public-benefit facility was initiated by a grant from the National Science Foundation (NSF) and is led by bioengineers from UC Berkeley and Stanford University…
BioFab projects will be designed to produce broadly useful collections of standard biological parts that can be made freely available to both academic and commercial users, while also enabling the rapid design and prototyping of genetic constructs needed to support specific needs of partner efforts such as SynBERC Testbeds. The BioFab will thus also represent the first significant focused investment in the development of open technology platforms underlying and supporting the next generation of biotechnology. Once fully operational the BioFab facility will be capable of producing tens of thousands of professionally engineered, high quality standard biological parts each year."[7]

Chassis: Refers to the microorganism or cell-free system that acts as the framework or shell in which synthetic biology constructs are operated (e.g. *E. coli* and yeast).

CSAIL: Computer Science and Artificial Intelligence Laboratory at MIT (Massachusetts Institute of Technology), Cambridge, MA, US.[8]

CSynBI: The Centre for Synthetic Biology and Innovation (CSynBI) at Imperial College London and in association with London School of Economics and Political Science seeks to develop foundational tools for synthetic biology and generate applications for research, healthcare and industry. Alongside the technical research, CSynBI's partnership with BIOS Centre researchers

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[2] http://bbf.openwetware.org/.
[3] BioBrick(s)™ is an officially trademarked term, under the BioBricks™ Public Agreement (BPA). In the body of this thesis, the use of the term appears without the ™ symbol, with recognition of its official form given here. For proposed legal agreement on sharing BioBricks, see: http://bbf.openwetware.org/BPA.html.
[4] http://biobricks.org/faq/.
[5] http://partsregistry.org/Part_Types.
[6] http://partsregistry.org/Help:BioBrick_Assembly;
http://openwetware.org/wiki/The_BioBricks_Foundation:Standards/Technical/Exchange/Old_Discussion#Biobrick_Characterization.
[7] http://www.biofab.org/about.
[8] http://www.csail.mit.edu/.

from The LSE integrates science with emerging ethical, legal and societal issues in an attempt to mature this biotechnology responsibly.[9]

Design Interactions: A niche of speculative and critical design that explores roles, contexts and approaches in relation to (possible) social, cultural and ethical impacts of existing and emerging technologies.[10] Two of the field's most eminent pioneers are Professor Anthony Dune and Professor Fiona Raby of the Royal College of Art, where they run a masters program in this subject (both Daisy and James hold this MA). Interaction designers such as Daisy and James tend to work closely with practitioners of biotechnology to inform their work (expressed in prototypes, simulations, video and photography) that inspires reflection on potential future implications – positive and negative – of humans living in an increasingly technological world.

DIYbio: Do-it-yourself biology (DIYbio) is a sub-culture and organisation within the synthetic biology community that is "dedicated to making biology an pursuit for citizen scientists, amateur biologists and biological engineers who value openness and safety".[11]

Dry lab / work: refers to work on computers (e.g. modelling, Wiki edits), or on paper (e.g. mathematics, mind mapping).

iGEM: The International Genetically Engineered Machines Competition.

JCVI: J. Craig Venter Institute.[12]

Plasmid: a small, autonomously replicating, circular piece of DNA that exists in bacteria.

Promoter: a region of DNA that regulates the transcription of functional genetic units.

The Registry: Also known as The Registry of Standard Biological Parts,

Wet lab / work: refers to work on biological materials, with the researcher typically gloved and in a lab coat.

Note 1: Some quotations have been smoothed over to make them more comprehensible.

Note 2: The photos throughout this work are attributed to the author, Caitlin Cockerton, unless otherwise attributed in captions or footnotes. Photos are also aligned as best as possible given their size and other textual constraints in the formatting of this thesis.

Note 3: There are several website references throughout this work. For consistency and clarity in text, websites are referenced as footnotes in the body of this work. A full reference that includes holder of website and date accessed is provided in the Internet Reference list.

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[9] http://www3.imperial.ac.uk/syntheticbiology; http://www2.lse.ac.uk/BIOS/research/synbio/synbio.aspx.
[10] http://www.di09.rca.ac.uk/information.
[11] http://diybio.org/.
[12] http://www.jcvi.org/.

INTRODUCTION: GOING SYNTHETIC

In October 2007 at the LSE, a panel of eminent scientists and humanities scholars came together to discuss the social implications of an emerging biotechnology in an event entitled, 'Beyond the Genome: The Challenge of Synthetic Biology' (Debate 2008). At that time, the J. C. Venter Institute was attempting to construct a well-defined "minimal operating system for life" in a redesigned microorganism called *Mycoplasma genitalium*. The audience of lawyers, regulators, economists, ethicists, social scientists and members of the public had a number of concerns:

> What in fact is synthetic biology? And what impacts will it have? Are the projected possibilities of synthetic biology part of a fantastical future, or will these new technologies indeed transform our lives? (Debate 2008, 3)

Two and a half years later, in May 2010, Venter's group succeeded in constructing the first fully synthetic chromosome and operating it in a bacterial cell (Gibson *et al.* 2010). With that development Craig Venter received major media attention for himself and the broader field (Adams 2010; BBC News 2010; Cookson 2010; Economist 2010; Sample 2010; Wade 2010). Researchers at the J. C. Venter Institute have since focused on developing a synthetic organism that they hope may enable the production of a variety of biological products and renewable fuels.

The story of my motivation to examine this nascent biotechnology began at that LSE debate almost four years ago. As Sarah Franklin declared that evening, "We can never have a science that's outside the social" (Debate 2008, 10); furthermore, in the UK and other developed countries a secular, scientifically driven agenda is at the core of modern society. Franklin went on to celebrate and encourage a

continuation of the dialogue between scientists, sociologists and other interested parties – one that was not laden with hype and fear-mongering statements, but rather a conversation that afforded "room to think", with genuine empirical consideration of what it means to engineer synthetic life in the 21st Century (ibid, 13). Following that initial point of inspiration, I went on to write two related MSc dissertations: one which looked into early UK and EU policy discourses in comparison to the positions of UK pioneers in synthetic biology; and, the other, which examined the open source biotechnology movement. These explorations led to this doctoral work. However, before introducing my thesis' particular concerns, I would like to provide an overview of synthetic biology and some critical context.

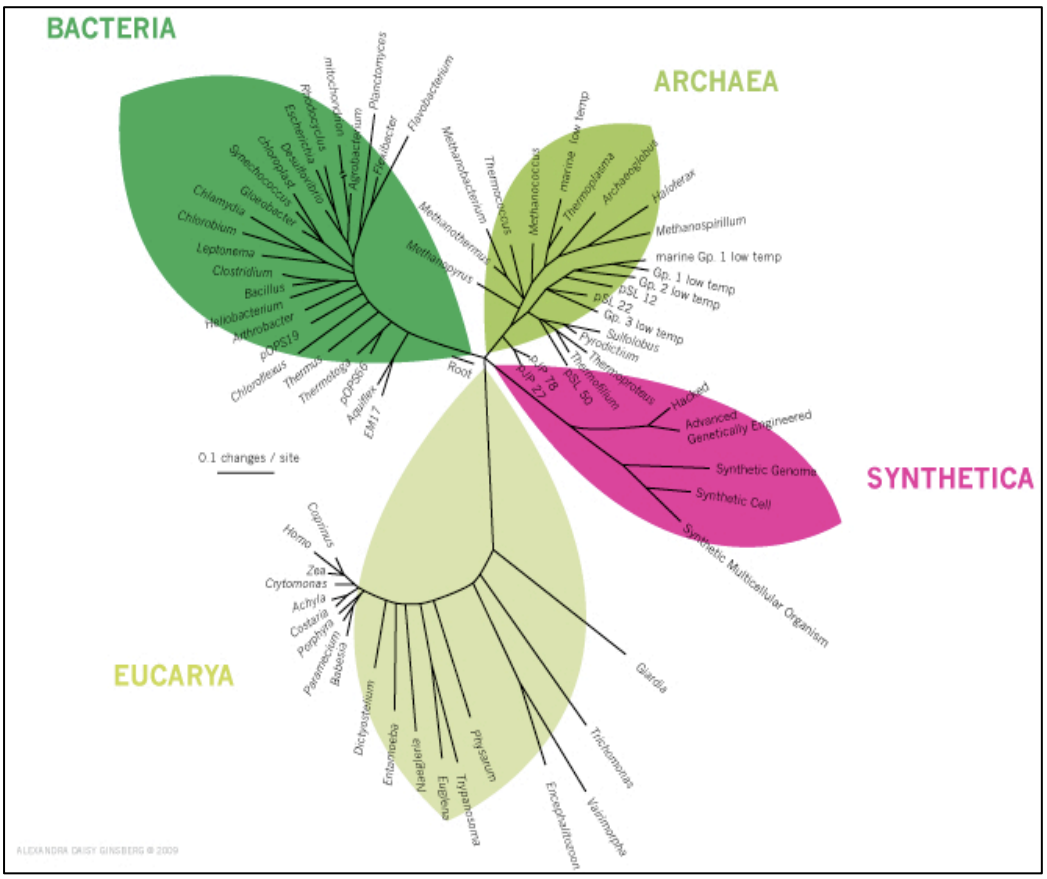
Imagine considering biology from the perspective of an engineer who is seeking to mine its incredibly complex, sensitive, reproducing and vast resources in order to design and build new living machines – this is the ambition driving synthetic biology. More precisely, practitioners of this field aim to make products and applications (such as sensor and remediator devices, medicines and biofuels[13]) that solve real world problems by sourcing, manipulating and piecing together functional components from microorganisms, plants and animals. Pioneers of this vision for engineering biology believe that we now know enough about genetic material so it can be used as building blocks – so called BioBricks[14] – for

[13] For further on synthetic biology applications, few of which have been realised but many held as future promises, see McDaniel and Weiss 2005; Adrianantoandro *et al.* 2006; Ro *et al.* 2006; Khalil and Collins 2010.

[14] "A BioBrick™ standard biological part is a standard biological part that meets the technical and legal standards set forth by the BioBricks Foundation (BBF). Each distinct BioBrick™ standard biological part is a nucleic acid-encoded molecular biological function (e.g., turn on/off gene expression), along with the associated information defining and describing the part" (http://biobricks.org/faq/).

systematically constructing well-characterised, discretely purposeful biological parts, devices and systems.[15] Interestingly, projects that subscribe to this school of thought require expertise from life sciences, engineering and other disciplines. Exciting as the philosophy of synthetic biology may be – with its reconfiguration of life as the 21st Century building material that might solve pressing global problems – the field's *grand ideas* are far from the present *reality*.

Figure I: The New Tree of Life



With this image, designer Daisy Ginsberg proposes adding an extra branch to the Tree of Life in order to categorise new living material emerging from synthetic biology:
"The Synthetic Kingdom is part of our new nature".[16]

[15] Definitions of synthetic biology are various and contested as different approaches to biological engineering (e.g. bottom-up, top-down and proto-cell construction) employ this brand (O'Malley *et al*. 2008; Rabinow and Bennett 2008). This branding, being part of the 'cutting edge', is an important funding strategy. This thesis focuses on the so-called 'parts, devices, systems' or 'engineering approach' (Endy 2005; Canton, Labno and Endy 2008; Purnick and Weiss 2009).
[16] http://www.daisyginsberg.com/projects/syntheticingdom.html.

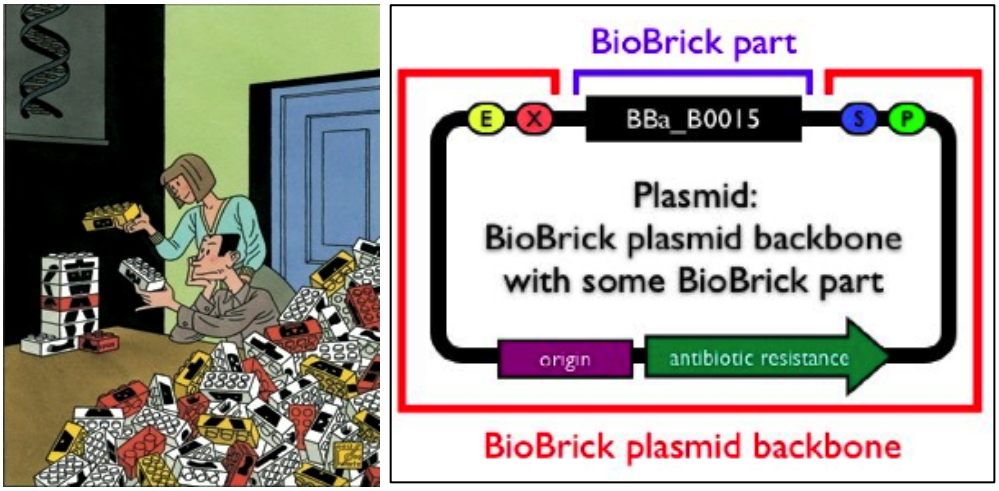
Synthetic biology faces a number of significant and interlinking challenges, making it a fascinating site for social study. These challenges are inherent in the biology that it seeks to engineer, present in the institutions where this research is practiced, embedded in the wider political and economic contexts and in the socio-cultural spheres in which techno-science always exists. This is a locus where claims about a burgeoning biotech revolution are constantly made and disputed; a site where big egos, brilliant minds, academic laboratories and private institutions compete for funding; where a 'new breed' of idealistic and socially mindful young scientists and engineers are trying to drive this technology through an open source framework for sharing DNA parts, rather than clamping down on research innovations by concealing and patenting; this is a world where scientists in their garage believe they are pioneering a kind of radical movement to 'bring science to the people' through 'Do It Yourself Biology' (DIYbio)[17]. At this point, we cannot know whether synthetic biology will lead to the construction of completely synthetic organisms that function as generic production machines where, with the swapping of a few components, the output could be a medicine, a material or a biofuel; neither can we know whether the current research into cancer-eating bacteria will be effective; nor can we anticipate that biology will eventually get so easy to engineer that it becomes part of childhood play (the 'Lego™ of the future' as some speculate). In what are still early days, synthetic biology's definitions, principles, practices and culture are in-the-making.

I'll begin with technical difficulties in engineering biology. Living systems and their component parts have incredible molecular complexity, stochastic behaviour

[17] See http://diybio.org/about/. A selection of media references support these claims: Jan 2006; Pollack 2006; Morelle 2007; Ahuja 2009; Economist 2009; Harmon 2009; Henderson 2009; McFadden 2009; Specter 2009; Whalen 2009; Mooalem 2010.

patterns, and a capactity to evolve and generate emergent properties – these characteristics pose a number of challenges to synthetic biologists as they struggle to work with building materials that are far from the reliable, robust, predictable ideal. Even though described and visualised as BioBricks that 'snap together, like Lego™', biology is simply not a material of engineering like the bricks and mortar of buildings or bridges (see Figure II). Similarly, biology is not analogous to the build-up of electronic circuitry where resistors, capacitors and transistors can be constructed in a standard way to produce computers and networks (Figure III). Nonetheless, many synthetic biologists like to think in such parallels and there is an abundance of supportive imagery that is flashed up in presentations and in the media.

Figure II: BioBricks associated imagery[18]



[18] From top left, three images are sourced from: Spector 2009; http://partsregistry.org/Assembly_standard_23; http://partsregistry.org/Catalog.

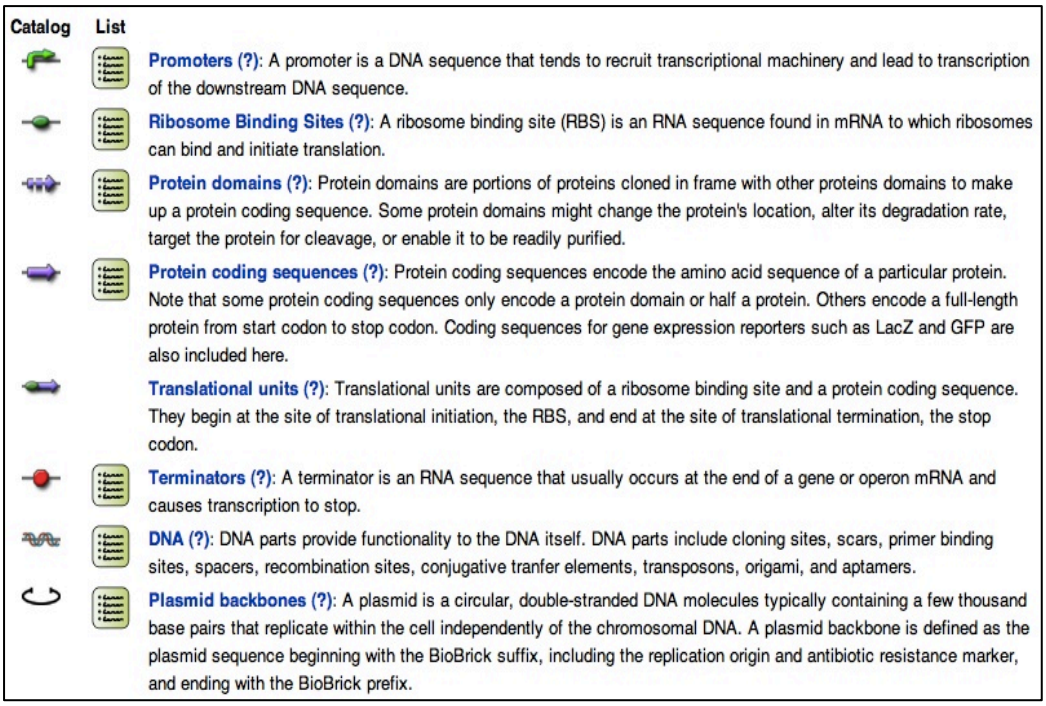
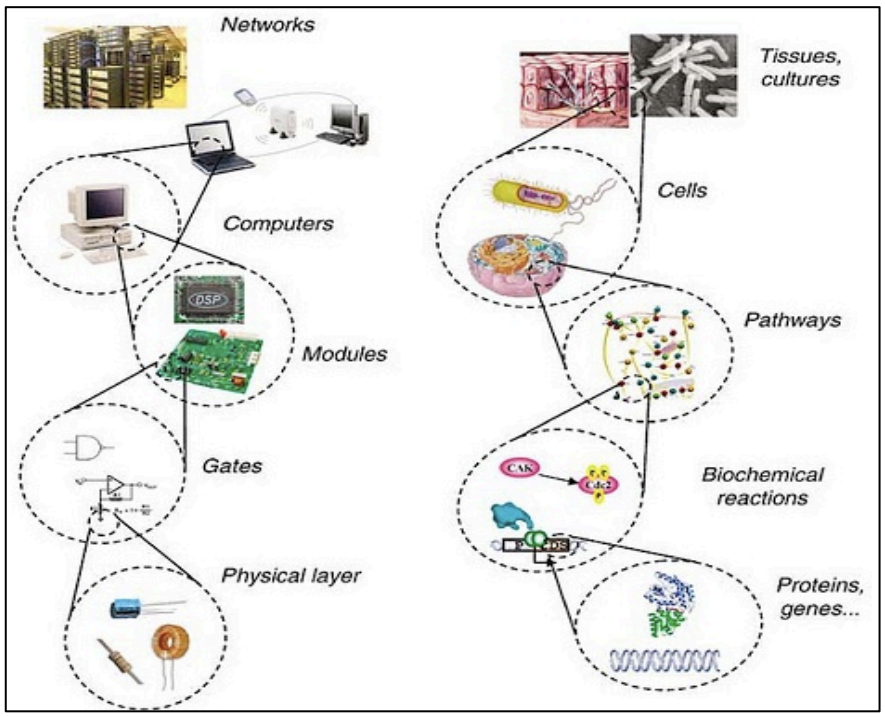


Figure III: Biology as parallel to electronics engineering[19]



Most recently, the technical challenges to synthetic biology have been summarised in "five hard truths", namely that (1) biological parts are difficult to

[19] Image sourced from: http://nextbigfuture.com/2006_05_28_archive.html.

define and characterize; (2) biological circuitry is unpredictable; (3) complexity in living systems is unwieldy; (4) biological parts that are human-made constructs often don't fit well together; and (5) variablity in living systems tends to crash the desired circuit construction (Kwok 2010). Other biologists present convincing arguments that confront synthetic biology's reductionism in celebrating biology as a study of complex, evolving organic material (Woese 2004; Mazzocchi 2008); such papers condemn the notion that biology can be understood in simple, mechanical terms and advocate that those points of view miss the idea of what is most special about the living world. Biology (in Woese's view) is the most wonderous and elusive of sciences – our representations of the living world will only ever be partial. Moreover, for Woese, biologists ought to be utterly fascinated, and *humbled*, by the incredible phenomena they seek to understand, and ought not to think it possible to *engineer* life (at least, not on the scale synthetic biology sometimes proposes). Far more dated views coming from vitalist[20] traditions pose similar challenges to synthetic biology's philosophy. Canguilhem (2009) reminds us that life resists mechanisation and that organisms must be considered with respect to survival in a milieu. For Canguilhem (2009), the prevalence of vitalism throughout history lends proof-worthy quality to the idea that living organisms are more than the sum of their parts. The non-mechanical, *special* nature of biology – its *messiness* that "gets in the way of the engineering" (Kwok 2010, 288) – are important themes that will be revisited throughout this thesis.

[20] In very basic terms, vitalism says that biological systems are not reducible to purely physical and chemical mechanics.

Leaving technical difficulties, let us acknowledge that some elements of biology can be thought of from a reductionist and mechanistic perspective to allow the rational design and building of novel synthetic living systems, albeit relatively simple ones at present.[21] However basic intentionally engineered biological clocks, switches, oscillators and feedback loops may sound, proponents of synthetic biology often argue that there is great potential for the field to eventually develop into a full-fledged industry, even constitute a "third industrial revolution" (Royal Society of Chemistry Science and Technology 2009). Such advocates would add that the path of creating an industry based on building with biological parts may be thought of as analogous to trajectories witnessed in the synthetic chemistry or electronics industries – these highly economically valuable fields, they point out, started with characterising basic parts (elements and compounds, or resistors and transistors). Of course, promissory parallels – for instance, *synthetic biology parts will eventually lead to a great number of industry applications (e.g. from biofuels to bioremediators), just as synthetic chemistry research eventually led to a vast range of materials and products (e.g. from rubber to pharmaceuticals)* – are called upon with the emergence of any research field that needs to trade promises of future financial gain for present funding.

As it stands, the state of functioning synthetic biology applications is limited – though several parts or systems are claimed to be *on their way to…*, in my view, the number of systems that feasibly look like they might turn into a 'consumable' within the next five years are probably counted on one hand. What has been called the poster child work of synthetic biology has been carried out in Jay Keasling's

[21] A number of synthetic biology articles explain functional success of engineered biological clocks, oscillators, switches and feedback loops (e.g. McDaniel and Weiss 2005; Tyson *et al.* 2008; Purnick and Weiss 2009; Tigges *et al.* 2009; Danino *et al*. 2010; Fussenegger 2010).

laboratory at UC Berkeley; there, scientists and engineers have been working for almost ten years to make microbes that produce the antimalarial drug artemisinin.[22] This has been one of the most extensive, expensive and successful research and development efforts in the field (though still in the pipeline with its projected commercial distribution in 2012). The Keasling laboratory has followed the artemisinin project in taking up the challenge to engineer microbes that produce biofuel. We await the outcome of this endeavour.

With at least one very exciting, tangible application to point to, synthetic biology advocates have, over the last few years, been actively promoting the vast potential "biovalue" that this field could generate. There are hyperbolic arguments along the lines of, 'just look at what Keasling has done – completely re-engineered and refined a biological pathway in order to treat malaria…. The ways that biology can be re-designed and re-engineered to solve major world problems are endless!' Biovalue, however, is a term that has been used often in social studies of techno-science; in this tradition, one appreciates the kinds of complex socio-political networks within which biovalue operates. This useful concept began with Waldby's (2002) definition:

> Biovalue refers to the yield of vitality by the biotechnical reformulation of living processes. Biotechnology tries to gain traction in living processes, to induce them to increase or change their productivity along specified lines.... This intensification of leveraging of living processes typically takes place not at the level of the body as a macro-anatomical system but at the level of the cellular or molecular fragment, the mRNA, the bacterium, the oocyte, the stem cell. (309-10)

Scholarship around this topic after Waldby's introduction (e.g. Franklin 2003; Hilgartner 2007; Rose 2007), shows that the concept of biovalue can be enlarged,

[22] Keasling (2009); http://keaslinglab.lbl.gov/wiki/index.php/Main_Page.

mapped out at multiple sites and intertwined with a range of dynamic factors: investor confidence, consumer hopes and fears, promissory visions and hyped up claims, credibility in science, trust in government, public understanding of science, cultural values and beliefs. Without going into detail here, I state rather plainly that with synthetic biology's trading on biovalue, inevitably there exists a political complex that ties into national economic agendas, various structures of governance, private and public monies, popular opinion, a code of ethics and so on. I am trying to convey a sense of the complexities and challenges that shadow synthetic biology's emergence; so, I ask for the reader's patience, knowing these generalisations will gain substance in later chapters.

As this work focuses largely on a UK context, I briefly indicate the high levels of political and economic interest in synthetic biology in this country. Consider the following extract from a recent policy document that demonstrates a political priority to stake a place for the UK as an international leader in this biotechnology:

> We found good indications that the UK is learning from past experiences in bioengineering when handling new emerging technologies, such as synthetic biology. The Government and Research Councils have recognised the value of synthetic biology early, and are providing funding. There is good activity in public engagement on synthetic biology. However we are concerned that while research is well funded there is not enough forethought about synthetic biology translation, for example developing DNA synthesis capability, which would provide the UK with an excellent opportunity to get ahead internationally. If this is not addressed, synthetic biology runs the risk of becoming yet another story of the UK failing to capitalise on a strong research base and falling behind internationally. (House of Commons Science and Technology Committee 2010, 3)

Looking at the growing number of UK synthetic biology networks and laboratories reinforces the message that researchers are becoming aware of the

substantial political and economic force invested.[23] Most notable, perhaps, is the recent establishment of the Centre for Synthetic Biology and Innovation (CSynBI) that partners Imperial College London researchers to social scientists from BIOS at the LSE; CSynBI was funded (around £5M) by an Engineering and Physical Sciences Research Council (EPSRC) Science and Innovation award that specifically aims to support new "areas of national strategic importance" and, indeed, the Centre is hoping to develop into a leading synthetic biology facility. Other significant research efforts have been underway for a few years at University of Cambridge, University of Edinburgh and University of Sheffield, with the list growing (footnote 23). Furthermore, a sample list of funding bodies that support UK synthetic biology research includes the Wellcome Trust, Biotechnology and Biosciences Research Council (BBSRC), Engineering and Physical Sciences Research Council (EPSRC), Royal Society, Royal Academy of Engineering, Royal Society of Chemistry, Medical Research Council (MRC), New and Emerging Science and Technology (NEST) group, Economic and Social Research Council (ESRC), Arts and Humanities Research Council (AHRC). Since the time I started researching synthetic biology in 2007, I have witnessed the funding opportunities grow rapidly in the UK; this growth comes with increasingly competitive stakes and a stronger push to form 'new and improved' alliances between science and engineering communities, social scientists, policy bodies and those in the field of interaction design.

[23] An incomplete sample list of UK synthetic biology laboratories, research centres and networks: http://www.synbiostandards.co.uk/index.php; http://sysos.eng.ox.ac.uk/control/RoSBNet/index.php/Main_Page; http://www2.lse.ac.uk/BIOS/research/synbio/synbio.aspx; http://www3.imperial.ac.uk/syntheticbiology; www.biochem.ucl.ac.uk/synbion/; www.bris.ac.uk/scn/; www.sheffield.ac.uk/synbio/home.html; www.synbiont.org/.

UK synthetic biology practitioners know that in order to be competitive in grant applications, there ought to be consideration of 'social and ethical implications' in most proposals. In part, this upstream inclusion of social and ethical issues, is tied to the notion of *learning from the past* (as quoted above, from the House of Commons); it is commonly held among UK synthetic biology stakeholders that, in order for the field to enjoy future mainstream success, the research community ought to do all it can to 'avoid another GM'.[24] Hence, it has become commonplace that most UK synthetic biology networks and research centres seek out an affiliation with social scientists (that is, with scientists and engineers inviting social scientists in), hoping that this may be a way to help consider social implications and lead to forms of governance that somehow lessen the risk of public backlash. This invitation to join a synthetic biology team has put a number of UK social scientists in a tricky position – on the one hand, they are often delighted to be granted open access to an interesting field of study; on the other, they feel uneasy about the extent to which they can do proper social science research, given their funding sources and implicit pressure from some synthetic biologists to legitimise their work, rather than seek genuine forms of collaboration. The complex relations that are developing across such disciplinary boundaries is an issue that cannot be substantively addressed here; however, they have been explored in recent publications (Calvert and Martin 2009; Macilwain 2009; Schuurbiers and Fisher 2009) and will also be explored to some extent throughout this thesis.

[24] Referring to the 'GM crisis' where public rejection of genetically modified foods was seen across the UK and Europe in the late 1990s and early 2000s (Gaskell *et al.* 2003).

Before turning more to this work's particular focus, it is important to note some of the content of the social and ethical issues. However, I must add a caveat: the meanings of these commonly cited issues are far more complex than I reveal here and there are many developing social dynamics that I cannot address in this brief overview. From 2007 and into 2009, the key social and ethical challenges in synthetic biology (mainly referring to UK and European contexts) generally consisted in a list of five or so standard topics. Not wishing to dwell on this overly rehearsed list, I provide the following summary chart and references:

Figure IV: Commonly cited social and ethical challeges in synthetic biology

	Commonly cited concerns	**References**
Biosafety	Accidental or intentional release of microorganisms into the environment could have unexpected consequences as synthetic organisms interact with surroundings and possibly evolve unpredictably.	NEST 2005; HSE 2007; Balmer and Martin 2008; POSTnote 2008; Schmidt *et al.* 2008; IRGC 2009; Lentzos 2009; Nuffield Report 2009; Schmidt *et al.* 2009
Biosecurity / Bioterrorism	The ability to construct new, modified or already existing microorganisms to use for malicious purposes is a threat. The increasing capacity to design and order DNA online from synthesis companies, in combination with a growing community of 'do-it-yourself biologists' practicing 'garage biotechnology' are a significant worry and difficult to regulate. A biosecurity threat is conceivable at both state- and individual- levels.	NEST 2005; HSE 2007; Kelle 2007; Balmer and Martin 2008; POSTnote 2008; Schmidt *et al.* 2008; IRGC 2009; Lentzos 2009; Nuffield Report 2009; *Schmidt et al*. 2009
Patenting; **Commercial vs Public Good**	The commercial potential of synthetic biology applications has led to concern that patents and monopolies could inhibit basic research and progress in the field. An 'open source' movement has responded to worries over burdensome patent thickets; for instance, the BioBricks Foundation (BBF) is a significant initiative working to facilitate an open research commons. Experts suggest both patent and open source frameworks are needed, but no uniform resolution yet exists.	NEST 2005; Balmer and Martin 2008; POSTnote 2008; Schmidt *et al.* 2008; Lentzos 2009; Nuffield Report 2009; Schmidt *et al.* 2009
Trade and Global	With the development of synthetic	NEST 2005; Balmer and

Justice	chemicals to replace cumbersome isolation and manufacture of naturally exisitng compounds (e.g. from plants), critics argue that synthetic biology could destroy local production in developing countries, thus maintaining the gap of health and wealth between rich and poor countries.	Martin 2008; POSTnote 2008; Schmidt *et al.* 2008; Lentzos 2009; Nuffield Report 2009; Schmidt *et al.* 2009
'Playing God'	The promise that synthetic biology might create 'artificial life' or is about the 'design and construction of synthetic life forms' has evoked fears that practitioners of synthetic biology might be 'playing God'.	NEST 2005; Balmer and Martin 2008; POSTnote 2008; Schmidt *et al.* 2008; Lentzos 2009; Nuffield Report 2009; Schmidt *et al.* 2009

I have found that by 2011, discussions around such social, political, moral matters and beyond have become far more sophistocated than they were previously.[25] Despite glossing over this list, UK synthetic biology leaders deserve recognition for their initiatives in opening up several arenas for questioning and debate.

With that introduction and brief context around synthetic biology, it is clear that there are many avenues that might be investigated sociologically and I have had to make some choices as to the focus of the present study. This thesis does not take place at a macrosocial scale – it is not concerned with, for instance, how governments might regulate synthetic biology or how various publics perceive this technology (though these are certainly pertinent matters). This thesis is also not historical, in the sense of looking back and tracking when and how synthetic biology came into existence (an interesting topic with deep historical, philosophical and literary roots that merit contestations about the field's 'newnness').[26] Further, while I draw on participation, observation and interview

[25] An LSE event in November 2009 ('Creating the organisms that evolution forgot - An 'Any Questions?' debate on synthetic biology'), meetings at the Royal Society and a set of gatherings among a network of UK social scientists examining synthetic biology have all encouraged a more informed and rich debate than I observed upon first studying this field.

[26] Points of debate on this issue can be found in referring to Leduc (1911), Loeb (1912), Szybalski (1974) and Serrano (2007).

data, this thesis is not a laboratory ethnography that prsues an argument for the construction (or the 'social construction') of scientific 'facts'.[27]

This thesis is, however, situated within the broad field of sociology (and philosophy) of scientific knowledge. I therefore discuss some key aspects from this extensive body of work in Chapter 1, focusing in particular on those that are relevant to the argument that will be made in this thesis – that is to say, those which I draw upon, and those which I depart from in significant ways. Above all, this work is empirical in its focus as I was a participant and an observer in the work of two small, but influential, groups of scientists and engineers as they helped to lay the groundwork for developing synthetic biology in the UK. In my account of this journey, the reader is invited into an exploration of how synthetic biology practitioners actively construct new forms of knowledge and life. I detail the practices and processes of *going synthetic* that is considering living materials not only as something to decode, understand, mutate and utilize for human ends, but also something to design, assemble from scratch and engineer into precise machines.

Gradually coming to the exact research questions addressed, I must first explain another layer of the empirical site that I have found most fascinating – the International Genetically Engineered Machines competition (iGEM)[28]. Having already given a flavour of several complexities ranging from those inherent in the biology to those in socio-political realms, it is apparent that the development and flourishing of a prosperous synthetic biology *industry* is far from certain.

[27] As in Latour and Woolgar (1986) or Knorr Cetina (1981), discussed further in Chapter 1.
[28] http://2009.igem.org/About.

However, many eminent synthetic biologists believe that iGEM is a locus of particular importance for the field's future as it is designed to inspire and teach a next generation of synthetic biologists. iGEM began in 2003 when its creators[29] decided to challenge a small group of MIT undergraduates, over the course of a month-long Independent Activities Period, to make improvements to a biological oscillator, a microbiological machine that acts like a time-keeping device and appears as blinking cells.[30] From this mini design course grew a summer competition of five American teams in 2004, 13 (international) teams in 2005, 32 teams in 2006, 54 teams in 2007 and 84 teams in 2008. In 2009 – the year in which I conducted my fieldwork – iGEM had over 1200 participants in 112 teams from five continents and the competition had almost out-grown the space limitations of residing in parallel sessions in MIT's six largest auditoriums. Interestingly, by 2009 iGEM had also collected a substantial list of supporting corporate biotech companies as well as other sources of national and institutional funding – including financial backing from the FBI.[31] Not surprisingly, the media attention around iGEM – with its reputation as a source of budding biotech ideas and practitioners – was also a significant feature (Bland 2009; Ginsberg 2009; NPR 2009; Smolke 2009; Mooallem 2010).

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[29] Tom Knight and Randy Rettberg of MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL), and Drew Endy from (at that time) MIT's Biological Engineering Division. (Endy is now Assistant Professor of Biological Engineering at Stanford University.) Importantly, this group of very successful computer scientists and engineers rather like to be thought of as 'big kids' who like to 'build stuff'.

[30] Interestingly, the inspiration for the iGEM competition can be traced back to a course on electronic circuit design taught at MIT by Lynn Conway that started in 1978 (Carlson 2010, 82). Owing to a rigorous abstraction hierarchy and decoupling of design and fabrication that was easy to adopt, this course led to the international dissemination of very large systems integration (VELSI) circuit design (ibid). The success of this model strongly influenced developers of iGEM.

[31] iGEM 2009 partners: The MathWorks, GENEART, SynBERC/National Science Foundation; sponsors: Invitrogen LIFE Technologies, Federal Bureau of Investigation; affiliates: MIT, BioBricks Foundation, Institute of Biological Engineering (http://2009.igem.org/Sponsors). Additionally, 2009 iGEM teams were sponsored by other biotech companies and corporate sponsors – too many to name here. For example, see Cambridge iGEM team Wiki.

Every year this competition challenges university teams of approximately six to ten top-performing undergraduates from across life science and engineering disciplines[32] – supervised by a few eager PhD students and faculty – to craft a genetic machine using a database of BioBricks.[33] Teams typically design and build their bio-machine over a period of three or four summer months before competing at the iGEM Jamboree held at MIT in November. The clever business-like aspect of iGEM is a requirement that teams not only use a particular standard of part-assembly and characterisation, but also contribute back to The Registry of Standard Biological Parts, thereby continually growing the library of BioBricks and supporting synthetic biology's greater development. In brief, this competition works to (i) inspire and specifically train a possible next generation of synthetic biology practitioners; (ii) encourage the growth of knowledge as well as a central database of biological parts that significantly helps the field's advancement; (iii) seed the development of several academic synthetic biology laboratories and even some start-up biotech companies; and (iv) symbolise a number of fundamental principles and ideologies of this field, both technically and socially.

Finally, then, this work aims to (i) illustrate a process of knowledge and material production, situated in the practices and processes of developing scientists and engineers as they undertake the iGEM challenge, and (ii) assess the significance

[32] Typically, students undergo a selection process to 'make the team' – CV's, lab skills, maths ability, computer skills and general social demeanour are evaluated (see Chapter 3).
[33] BioBricks come from The Registry of Standard Biological Parts. Noting the description on the website: "The Registry is a continuously growing collection of genetic parts that can be mixed and matched to build synthetic biology devices and systems. Founded in 2003 at MIT, The Registry is part of the Synthetic Biology community's efforts to make biology easier to engineer. It provides a resource of available genetic parts to iGEM teams and academic labs" (http://partsregistry.org/Main_Page).

of iGEM as an interesting social 'tool' that is striving to support synthetic biology's future flourishing. I address the following research questions:

- How do teams of scientists and engineers imagine, design and build new living systems? What tools for thinking and doing do they employ in this process?
- In this process of knowledge and material production in synthetic biology, how do young researchers transition and rationalise the gaps between the imagined, the designed and the real microbiological machines that they craft?
- How does an undergraduate competition at the heart of synthetic biology seek to ensure the future flourishing of this emerging biotechnology?

The empirical study conducted took place mainly in laboratories at the University of Cambridge and Imperial College London, but also at MIT, where participants embarked on the iGEM challenge. (Note that the thesis questions, aims, literature and methodology are fleshed out in greater detail in the next two chapters.)

The ways in which curious, eager students dream up ideas of living machines and turn them into material realities, as well as their resultant beliefs about this biotechnology after their iGEM experiences, reveals a great deal about the technical, social and cultural dynamics of this field-in-making. In investigating a microsocial sphere that is developing synthetic biology's tools, materials, values and practitioners of the future, this thesis opens an informed space through which one may begin to think about how, over the coming years and decades, new

engineering perspectives of biology and the living might percolate into society and culture more generally.

CHAPTER SYNOPSES

Chapter 1: *An inspired inquiry*

The research questions, aims and influential literature are discussed. Four main bodies of literature are explored: (i) *Sociology of scientific knowledge, laboratory studies, selected STS concepts;* (ii) *Intervening science and 'taking a look'*; (iii) *Synthetic biology-specific literature; (iv) Bachelard and Canguilhem*.

Chapter 2: *Following knowledge and material production in iGEM*

This chapter concerns research methodology. Relevant background about entry into the field and an outline of the narrative's substantive text are given. I explain how my role as an embedded social scientist developed as relations with participants in the field changed over time. Finally, I discuss modes of analysis employed in working with field-notes, interview data and visual material.

Chapter 3: *Dreaming up ideas*

Beginning the substantive chapters that take place in the 'home laboratories' of the University of Cambridge and Imperial College London groups, this chapter explores how each team came to dream up ideas for an iGEM project. I discuss the teaching of synthetic biology and illustrate practices and processes in the teams' brainstorming until they reached an idea that they could work with.

Chapter 4: *Evolving ideas*

This chapter details how disciplinary contestations, advisors' judgements, idea re-evaluations, experimental complications and trouble-shooting of problems all shaped the course of the two groups' biological machine projects. The ideas and

their representations that are discussed in Chapter 3 are shown to have evolved as laboratory work and computer modelling became the teams' central focus in the middle period of their projects. The exploration revolves around how thoughts were transformed, under the influence of intellectual technologies, applied tools, techniques and experiments.

Chapter 5: ***Making real***

This chapter explores what happened as the teams began to make tangible re-engineered biological entities. How shall we understand these forms of glowing or pigment producing bacteria? Taking Hacking's (1983) position as a 'realist about entities and an anti-realist about theories', I describe the reality of these new forms of living material and articulate why my conceptual analysis departs from social constructionist views.

Chapter 6: ***Selling ideas***

This chapter takes place mostly at the iGEM Jamboree, when thousands of competition participants descended upon MIT to showcase their synthetic biology creations to an international community. I explain how students demonstrated an ability to 'sell' their ideas, fitting their technical accomplishments into a particular set of social and political rules of the field.

Chapter 7: ***To join the club, or not***

Empirically, this chapter draws on interviews and informal conversations with students and leaders of the synthetic biology community in which they reflected upon the competition's impact. I explore iGEM's success as a tool to educate and

indoctrinate a next generation of synthetic biologists to develop the field. Follow-up stories illustrate where some of this study's participants went after a little time and distance from the 2009 competition.

Chapter 8 / Conclusion: ***Emerging waves in synthetic biology and beyond?***

The key arguments are summarised, outlining an informed space through which readers may better participate in current and future debates on engineering living forms. New questions arising in synthetic biology are opened up, inviting the reader to further levels of reflection.

1. AN INSPIRED INQUIRY

Nikolas Rose (2007) calls for scholars across social studies of life sciences to join forces in mapping a "modest cartography of the present" as a complex network of "molecular biopolitics" takes shape across several areas of biomedicine and biotechnology, interconnected with political, economic and social issues; operations in these networks bring us to question how 21st Century philosophies of life and the living are being shaped (5, 12). This inquiry takes part in that challenge, examining the operations of a microsocial sphere of scientists and engineers seeking to design and build living machines in 2009. This work is largely based upon empirical findings but I begin by describing my research questions and aims, as well as introducing the body of literature that originally inspired this investigation.

1.1 Research questions and thesis aims

Core research questions:

- How do teams of scientists and engineers imagine, design and build new living systems? What tools for thinking and doing do they employ in this process?
- In this process of knowledge and material production in synthetic biology, how do young researchers transition and rationalise the gaps between the imagined, the designed and the real microbiological machines that they craft?

- How does an undergraduate competition at the heart of synthetic biology seek to ensure the future flourishing of this emerging biotechnology?

I shall now elaborate each question, outline the courses that their answers follow and say a little about how they intertwine. The first set of questions are examined in Chapters 3 through 5, where I provide an empirical account of how teams went about imagining, designing and experimentally building synthetic biological machines. This content is *social*, *material* and *practical*. The *social* involves how synthetic biology is taught; how team dynamics evolve (e.g. with respect to leadership roles and organisational behaviour) and operate within hierarchical chains of affirmation; and how boundaries operate across disciplinary perspectives (e.g. dividing engineers and life scientists). For the *material* content of imagining, designing and constructing, I use photographic data to illustrate 'intellectual technologies' (Miller and Rose 1990) in operation – that is, the notion that dreaming up ideas is not just a matter of thought, but has a materiality in the use of 'tools for thinking' such as drawing diagrams, making lists, using computer programs and presenting. Many ideas that will be discussed began their material journey on paper as mind maps or online in brainstorming forums (Chapter 3); a select few ideas were then translated into laboratory experiments and processed further in computer modelling (Chapter 4); finally, some ideas evolved into real biological systems, ones with a functionality that could be visualised and / or measured (Chapter 5). Finally, the *practical* content of engineering a microbiological machine is explained in relatively non-technical terms and concerns how practices and protocols were carried out in experiments and

computer modelling. All three of these aspects – social, material and practical – are, of course, interwoven.

The second area of questioning – on transitioning and rationalising the gaps between the imagined, the designed and the real microbiological construction – is answered, in part, because these teams were on a forced timeline that would result in the final competition Jamboree (at the end of October, after about three to six months of intensive work). Although the direction of knowledge and material formation in synthetic biology projects is not linear – the three stages overlap and there is a re-circuiting (re-imagining, re-designing and re-building), as problems and troubleshooting feature in all biological laboratories – the forced conclusion of the competition meant that iGEM teams adhered to beginning-, middle- and end-stages, even though they do not necessarily flow smoothly. There are gaps and leaps to make in order to move from ideas, to experiments, to results, to bringing a competitive project to the iGEM finale. These are evident in Chapters 3 to 6.

The final research question is investigated with findings at, and after, the Jamboree when I realised how iGEM inspires students to really sell their ideas, while they are simultaneously being sold several ideologies of the wider synthetic biology community; for some, this 'selling' extends beyond the competition and links up to joining the 'synthetic biology club' (Chapters 6-7). In considering iGEM's role in synthetic biology's future, I point to examples where ideas from the competition have been plucked and pursued at key laboratories. There are many cases of iGEMers going on to further study in this field, in masters and PhD

programmes. Others, such as team advisors, are inspired by their iGEM journeys; one major trend has been advisors going back to their universities after the Jamboree and developing synthetic biology courses and some fully-fledged research centres. There are also several instances where teams are built first by keen students who then approach a member of their university faculty to ask for supervision; hence, sometimes iGEM students even teach themselves and faculty about synthetic biology. Often, successful teams return home and receive attention from their university and local press, and place another point on the international synthetic biology map. Overall, iGEM is the point of origin for many lines of development: development for individual students, some of whom may turn into future leaders of synthetic biology; development for institutions that do further work in this field; and, development for synthetic biology as an up-and-coming, global biotechnology.

1.2 Literature review

In this thesis I examine a process of knowledge and material production as I was an embedded participant/observer of the practices and processes of scientists and engineers as they undertook the iGEM challenge; I also explore the significance of iGEM as a 'tool' for social and cultural engineering that is striving to support synthetic biology's future flourishing. There is now a very large literature spanning over half a century of sociological and anthropological investigations of the activities of scientists as they go about their work. In this review of the literature, I have therefore been selective, and focussed on those contributions that – in their modes of questioning, conceptual and analytical frameworks – relate to this thesis. My aim is not to provide a comprehensive overview, but to consider

the works that have helped me to reflect critically on where and how this study fits in a landscape of sociology and philosophy of science scholarship. In the core chapters, I focus on providing new empirical richness (and also conceptual frameworks to fit that data), so it is here that I take the opportunity to highlight where some of this work's themes hold affinities with earlier works.

Sociology of scientific knowledge, laboratory studies, selected STS concepts

One of this work's core aims – to give an empirical account of knowledge and material production in a local site of biotechnological development – sits in a tradition of sociology of scientific knowledge (SSK).[34] I will focus here on those contributions that have relevance to, and made a contribution to, the way that I have approached this study.

Much contemporary sociology of scientific knowledge takes issue with the arguments made by one of the earliest sociologists to consider science – Robert Merton[35]. Merton, whose position is usually described as 'structural-functionalist', assumes that a well-functioning society is made up of unified, overarching institutions – religion, science, government, etc. "The institutional goal of science", according to Merton, "is the extension of certified knowledge" (1973, 270). Further, Merton argued that appropriate institutional conduct is guided by certain norms, whereby followers are rewarded and violators punished.

[34] This field of work has been rather controversial. For instance it is common to refer to 'the science wars' to describe about a decade of intense intellectual debate between scientific realists and postmodern critics (from STS, cultural studies, feminist studies and other disciplines) about the nature of scientific knowledge – one side believing it to have a real, objective nature, the other critiquing this notion of scientific objectivity from several angles (Brown 2001; Parsons 2003).

[35] Merton is considered a major predecessor of 'new' SSK, which largely reacted against the ideals he set out. 'New' SSK is generally considered to have emerged in the early 1970s with the Edinburgh strong programme (mostly identified with David Bloor, Barry Barnes and some of their colleagues). The Bath school (identified with Harry Collins) is also closely affiliated with the strong programme.

In the case of science, he identified four norms: universalism, communism (or communalism, as later renamed), disinterestedness and organized scepticism.

- *Universalism* requires that a claim made in science cannot depend on the identity of the person making the claim (their race, class, gender, nationality, etc.); science is impersonal and its tenets either true or false, regardless of whomever is behind the statements.
- *Communism* declares that scientific knowledge is commonly owned, where theories, proofs, discoveries, etc. are disseminated openly and freely to the science community. Rewards in science therefore come to those who rapidly publish, thereby promoting the overall goal of science by encouraging collective furtherance of knowledge.
- *Disinterestedness* demands that scientists keep their interests disengaged from the practices and judgements made in science. This norm is enforced in the social institution of science to avoid fraudulent behaviour (e.g. reporting false data), which, according to Merton is relatively rare in science.
- *Organized scepticism* is the notion that new scientific ideas are subject to rigorous, methodical communal scrutiny.

These Mertonian norms of science are “moral” and “social” in nature and although he considered that there were “cognitive” rules of science (regarding evidence, theory structure, etc.), he distinguished between social and technical domains of science, and chose not to treat the latter as a subject for substantial sociological inquiry (Merton 1973; Sismondo 2010).

Karl Mannheim, whose work is closely related to Merton's, also made important contributions to the early development of this field. His "relationist" view aimed to counter relativism,[36] and claim that knowledge can be created in a community, at a give time and in a given place (both subject to change), without being arbitrary. For Mannheim, even though certain things are true only in a space-time context, this does not make them any less true. Most important to the 'new' SSK movements that took off in the 1970s, Mannheim drew a distinction between scientific, social scientific and ordinary systems of knowledge (Lynch 1993). Mannheim claimed that some forms of knowledge in mathematics and the exact sciences were nonrelational, not bearing the mark of history (e.g. statements such as 2 X 2 = 4); knowledge in the social sciences, on the other hand, was always historical and social, though this did not inherently take away from its value or comprehensiveness; finally, ideologies of a religious, moral and political nature are grounded in community beliefs and practices, with both content and criteria for validity being "essentially situated" (ibid, 45-6). In part, the idea that mathematics and the exact sciences might be excluded from the scrutiny of sociology of knowledge helped to spur on what became known as 'the strong programme' in SSK.

Before turning to consider this 'strong programme', it is important to acknowledge the contributions that were made to this field of study by Thomas Kuhn, notably through his (1996 [1962]) *Structure of Scientific Revolutions*. His arguments, in outline at least, have become very well known, and though I will not examine them in detail here, a few points ought to be highlighted. Kuhn

[36] Crudely, relativism implies that points of view cannot have any inherent truth or validity, always only relative to a subjective set of perceptions.

argued that science does not proceed as a form of rational, steady progress, but rather shows periods of *normal science* disrupted by *paradigm shifts*. During normal science practitioners share a paradigm – a set of beliefs, theories, methods, exemplars etc. In these periods of normal science, scientists engage in *puzzle solving* in a regimented and mostly cumulative fashion, without questioning the basic parameters of the paradigm in which they work. However, anomalies and problems tend to accumulate until a *crisis* point is reached. At this stage, an alternative paradigm comes to the fore, often led by younger scientists, and a *revolution* and paradigm shift might follow. If that revolution succeeds and becomes the new accepted view, normal science and puzzle solving can resume. Importantly, in Kuhn's work, science communities are based on ideas and practices, not idealistic norms (e.g. like Merton's) and they are organized locally, from bottom-up, not striving towards a broad, sweeping goal. Kuhn's *Structure of Scientific Revolutions* helped in opening the door for arguments that social factors relating to the organization of scientific activity and thought itself are essential in shaping the nature of scientific activity, its forms of thought and practice, and its periods of stability and change.

In the 1970s this way of examining science was given a radical twist, as a number of sociologists, historians and philosophers developed the strong programme in the sociology of knowledge. This programme explicitly challenged the divisions between technical and social domains of science (with only the latter as a matter for sociological inquiry), seeking to not only understand the organisation of scientific knowledge but also its *content* (Bloor 1991 [1976]; Barnes and Bloor 1982). David Bloor outlines this school's "four tenets" as follows:

1) It would be causal, that is, concerned with the conditions which bring about belief or states of knowledge. Naturally there will be other types of causes apart from social ones which will cooperate in bringing about belief.
2) It would be impartial with respect to truth and falsity, rationality or irrationality, success or failure. Both sides of these dichotemies will require explanation.
3) It would be symmetrical in its style of explanation. The same types of cause would explain, say, true or false beliefs.
4) It would be reflexive. In principle its patterns of explanation would have to be applicable to sociology itself. Like the requirement of symmetry this is a response to the need to seek for general explanations. It is an obvious requirement of principle because otherwise sociology would be a standing refutation of its own theories. (Bloor 1991 [1976], 5)

The mission of this new form of SSK is stated explicitly from the outset of Bloor's (1991 [1976]) book:

> Can the sociology of knowledge investigate and explain the very content and nature of scientific knowledge? Many sociologists believe that it cannot. They say that knowledge as such, as distinct from the circumstances surrounding its production, is beyond their grasp. They voluntarily limit the scope of their own enquiries, I shall argue that this is a betrayal of their disciplinary standpoint. All knowledge, whether it be in the empirical sciences or even in mathematics, should be treated, through and through, as material for investigation. … There are no limitations which lie in the absolute or transcendent character of scientific knowledge itself, or in the special nature of rationality, validity, truth or objectivity. (Bloor 1991 [1976], 1)

With that powerful calling, a new territory was opened for sociological study.[37] Key to this approach was methodological symmetry. In earlier work on the social history of science, the tendency was to explain 'false' beliefs in terms of external or social factors, while 'true' beliefs were explained in internal and rational terms. However, the strong programme's methodological symmetry demands an agnostic

[37] By way of key case study referencing in this genre, socio-historical works such as Pickering's (1984) examination of differing interpretations of high energy particle physics experiments and Shapin and Schaffer's (1985) investigation of competing interpretations of vacuum pump experiments both offer exemplary strong programme interpretations of controversial scientific knowledge production.

view that considers both 'true' and 'false' beliefs in science to be equally open to sociological explanation (Sismondo 2010). This has been an important premise for SSK scholarship, enabling researchers to analyse scientific knowledge production without considering the present state of knowledge as in some way more truthful, factual or rational than that which has gone before. The strong programme's early days were especially marked by attempts to connect broad social structure and social interests to internal scientific judgements, contents and controversies. This usually entailed a macro-social conflict or theme being connected to positions taken within a smaller-scale scientific debate.[38] This approach became controversial within SSK itself, with a number of scholars, notably Latour and Woolgar, arguing that it was invalid to regard social factors as the unproblematic external determinants of scientific thought and practice.[39]

Laboratory Life became the exemplar for a whole series of later laboratory studies, but these took several different forms.[40] For the present purposes, I will focus on selected themes from some key studies that are relevant to my own work.

[38] An example of such a case study is MacKenzie (1978), in which differing social interests in Britain on the subject of eugenics are linked to an examination of controversy around how to best measure statistical association between 1900 and 1914.

[39] Note in this transition between discussing SSK's strong programme and laboratory studies that a number of progeny intellectual pursuits broke off from this school of thought. Lynch (1993) amusingly describes the programme's descendants as a "loose and extended" family whose "lines of ancestry are far from "pure"", marked by several episodes of heated "sibling rivalries" and "intermarriage[s] of themes and research initiatives" (82-3). This lineage is not comprehensively described within the limits of the present literature review; however, a more thorough overview of spin out SSK scholarship can be found in Lynch (1983, 82-102) and Sismondo (2010). Shapin's (1982) article is also of interest in its defence of SSK coming under attack by many philosophers and historians as he highlights the value of several SSK empirical studies.

[40] Beyond the laboratory studies discussed in the body of this section, I have sourced inspiration in style and form from multi-sited ethnographies such as Franklin and Roberts' (2006) insightful examination of pre-implantation genetic diagnosis and Lock's (2001) cross-cultural portraits of organ transplantation and criteria for death in Japan and North America. Traweek's (1988) ethnography of Japanese and North American particle physics communities that documents the construction of scientific truth, the role of women and differences in experimentalists and theorists; Knorr Cetina's (1999) comparative work that highlights the differences in epistemic cultures between a molecular biology laboratory and a high energy physics laboratory; and Helmreich's (1998) ethnography that brings the reader into the world of Artificial Intelligence have also been influential in developing my appreciation for the craft of this kind of research.

First, *Laboratory Life* (Latour and Woolgar (1986 [1979]), which follows a process of 'fact construction' in Nobel Prize winning Roger Guillemin's neuroendocrinology laboratory at the Salk Institute. Second, Karen Knorr Cetina's (1981) *The Manufacture of Knowledge*, in which she follows the day-to-day workings of a plant science laboratory at UC Berkeley. Third, Joan Fujimura's (1996) *Crafting Science*, which details the collective production of accepted knowledge in the field of proto-oncogene research. Each of these three studies adopts an ethnographic approach to observing and detailing the day-to-day practical actions, tools, contextual complexities and social life at particular laboratories – a task that this thesis shares. Each also has relevance for questions of (social) constructivism, as in different ways, each argues that scientific facts and artefacts are actively created in the practices and cultures of the laboratory, and can be studied as such, even in their most 'technical' forms. No part of scientific practice is 'asocial'. For reasons that I will discuss shortly, however, the debate about social construction is not central to my argument in this thesis.

Latour and Woolgar's (1986 [1979]) pioneering anthropological treatment of laboratory scientists as an alien tribe traces the journey of how a scientific "fact" (namely that "TRF is Pyro-Glu-His-Pro_NH_2"[41]) came to stabilize and count as reliable knowledge in the context of everyday laboratory practices. In this work, the anthropological probe "brackets" out any previous knowledge of scientific practice, naïvely asking questions to gradually work out his observations. Latour

[41] TRF refers to "Thyrotopin Releasing Factor", a tri-peptide chemical produced in the hypothalamus, essential in human metabolism. Latour followed the production of that "fact" as an anthropological probe (and also lab tech assistant, ergo participant) based in the laboratory that 'discovered' TRF's structure not through analysis, but rather through synthesis. These discovery methods were considered extremely innovative at the time and the consequences of great importance to research on human metabolism (with medical implications, etc.); for this, in 1977 Roger Guillemin and Andrew Scally were jointly awarded the Nobel Prize in medicine.

and Woolgar (ibid) famously use the concept of *literary inscriptions* to describe the laboratory's obsession with various forms of writing – writing on blackboards; preparing slides for presentation; constructing graphs, diagrams and charts; constantly "coding, marking, altering" (49). They also extend this concept, describing laboratory equipment (such as mass spectrometers and bioassays) as "inscription devices" that "transform pieces of matter into written documents" (ibid, 51). Inscriptions then, for Latour and Woolgar (ibid), are observed to become pieces of evidence for scientists, something durable, transportable, readily shared and consumed by colleagues. In later works, Latour (1986; 1987) develops the concept of a specialized inscription, which he calls an "immutable mobile" – objects which are *mobile*, *immutable*, *presentable*, *readable* and *combinable* (1986, 7). While this conception clearly relates to the processes that I observe in my own study, it is significant to point out that the inscriptions that I examine are not so immutable, and indeed change as they travel across time and space.

In this work, I encounter mind maps, written protocols and practices involving a range of equipment and technologies; however, I do not use either the concept of *inscriptions* or that of *immutable mobiles* to characterise them. Certainly, the idea that scientific knowledge production essentially involves progressive inscription practices (e.g. from blackboard scribblings, to experimental protocols, to the making of tables and graphs, to the production of scientific papers and text books), each layering upon one another in a process of *materialization* or *reification* (Latour and Woolgar 1986), resonates with my own observations. However, I find it less helpful to unify all of these stages under the heading of 'inscriptions'. Further, the notion of *immutable mobiles* doesn't quite fit in

analysing the field of synthetic biology where inscriptions and descriptions of existing entities and practices, new hypotheses, new entities are all understood as essentially *mutable*. The very core of synthetic biology's proposal is that all biological entities, and our ideas of what we can create with their micro-components, are open to change; open to disassembly and reassembly that is only bound (hypothetically) by the imaginations of those who perform this kind of biological engineering. For these reasons, I have chosen a different approach, taking the vast amounts of visual, audio and written data gathered in my study and developing appropriate concepts for their analysis. That is to say, I chose to immerse myself in the data, and develop the concepts and draw out themes that I felt most relevant to this specific study. My methodological choices are further elaborated and substantiated in Chapter 2.

Let me now turn to Knorr Cetina's study (1981). She points out how "truth", "nature" and "theories" (what may commonly come to mind in thinking about scientific knowledge) are actually quite difficult to find in everyday laboratory existence. The laboratory is a localised place, notoriously contingent and circumstantial, where practitioners artfully modify situated scientific practices in the quest for "success" (not "truth" or "fact").

> The scientists' vocabulary of how things work, of why they do or do not work, of steps to take to make them work, does not reflect some form of naïve verificationism, but is in fact a discourse appropriate to the *instrumental manufacture* of knowledge in the *workshop* called a "lab". Success in making things work is a much more mundane pursuit than that of truth, and one which is constantly turned into credits in scientific everyday life via publication. Thus, it is a success in making things work which is reinforced as a concrete and feasible goal of scientific action, and not the distant ideal of truth which is never quite attained." (Ibid, 4)

Knorr Cetina (ibid) uses *tinkering*[42] and *making things work* as concepts that more accurately describe what scientists must do in their construction of scientific knowledge.

> It is the scientists' knowledge of what is a problem and what counts as a solution, educated guesses about where to look and what to ignore, and highly selective, expectation-based tinkering with the material that guides them toward an "innovative" result. (Ibid, 12)

Fujimura's (1996) study, *Crafting Science*, also demonstrates the ways in which scientists focus, not so much on questions of truth and falsity, but on creating and solving problems and making things work. She describes how scientists articulate *"doable" problems* – "the *process* of solving a problem from beginning to end" (Fujimura 1996, 10) – using a case study in which researchers in a private laboratory construct a problem involving antibodies that seemed to counteract the effects of oncogenes (ibid, Chapter 7). Fujimura shows how a research program was laid out; how keeping sponsors and funders happy, as well as incorporating marketing strategies, played into the process; how the experiments succeed and failed at different times; and how a division of labour was carried out. My own analysis, in Chapters 3 through 5, though framed in different terms, demonstrates a similar process, showing how *"doable" problems* are constructed and worked through in the iGEM context.

A second relevant aspect of Fujimura's (1996) study is her focus on *standardization* of theory and methods, which she argues runs alongside the growth of proto-oncogene research. Fujimura observes how previous conceptions of objects and theories such as genes, cancer, tumours, normal and abnormal

[42] Knorr Cetina's use of *tinkering* is much like Latour and Woolger's (1986 [1979]) use of the term *bricolage*, both relating to the sense in which the unruly materials and results of scientific practice are arranged, rearranged, negotiated and made to fit into the scientist's expected or desired view of things.

growth, which had been used variably across different fields, get reformulated in a collective fashion (though not without conflict). Moreover, she shows how the technical standardization of tools, technologies and practices (e.g. the use of the transgenic OncoMouse, recombinant DNA technologies, cloning procedures, etc.) is essential in the *co-construction* of a robust theory of oncogenes – the scientists' own shifting framing of research in this area as well as the very tools that they use are involved in a collective creation. She also notes how pioneers of oncogene research had to strike "a productive balance between novelty and standardization" (Fujimura 1996, 9). My own study demonstrates that, in the case of synthetic biology and the practices of iGEM teams, very similar issues of standardization prove to be central to the success, or otherwise, of the process.

Each of the laboratory studies I have described also considers the end products of scientific knowledge production. Latour and Woolgar (1986 [1979]) refer to an *inversion* happening at the end of the scientific research process. After early stages of doubts, contingencies, disagreements, changes in hypotheses and method, re-experiment, etc. – all evidently under the agency of scientists – when all is said and done, reality and solidity get attributed to the fact(s) and agency in making the fact is denied. Nature (as science's subject) and engineered products (as possible fruits of scientific research) are 'orderly' and that order must be restored at the end of a messy process – hence, the necessity of *inversion* (ibid). The reader will find in this thesis that a similar re-ordering of messy experimental processes and incomplete results takes place when iGEM students present their achievements on an international, competitive stage to conclude their work.

Both *Laboratory Life* and *The Manufacture of Knowledge* explore the importance of publishing scientific papers and attaining peer validation, credit and acceptance as ends of scientific knowledge production – a highly political and social activity at that. Knorr Cetina (1981) argues that scientific practices are re-crafted into research papers – a process that disconnects the active makings of science and presents the objectivist, ideal and tidy vision of a scientific achievement. Publication, marketing strategies and details of how a local scientific investigation fits into a wider, competitive economic funding structure are also explored in Knorr Cetina's (ibid) work, helping her build towards the challenging argument that there should be no distinction between social and natural sciences. While I do not follow this general line of argument in the analysis conducted for the present study, we will see, more specifically, that similar processes of marketing and presentation play a crucial role in stabilizing and objectifying the results of the work of the iGEM teams that I follow.

A further relevant aspect of Fujimura's (1996) study is her description of the creation of what she terms the oncogene research '*bandwagon'*. This *bandwagon* is a configuration held together primarily by the standardization of experimental systems, tools and packages that enabled practices and theories to be shared and passed between participants across several social and disciplinary spheres.

> The proto-oncogene bandwagon represents a particular configuration of events, actions, and situations through which cancer and cancer research worlds have been reconstructed. The multitude of commitments to oncogene research does not establish the fact that proto-oncogenes play significant roles in causing human cancers. Excitement and enthusiasm over a particular research program do not necessarily mean that theory is accepted… However, the sustained commitments and the continued momentum of oncogene research long past its initial emergence is one sign of the stabilization of the oncogene theory. (Fujimura 1996, 226)

The reader will see parallels between the processes described in the present study and Fujimura's account of the role of laboratory practices and activities that helped unite commitments under the prevailing oncogene bandwagon. I similarly detail lab practices and standards that enable a kind of synthetic biology bandwagon; additionally, in Chapters 6 and 7 of this study, one observes a kind of social and political rallying that is crucial to the processes of 'selling ideas' and choosing to 'join the club, or not'.

One of the abiding issues that have been debated in STS concerns 'social constructionism' – the claim that this or that fact, theory, piece of evidence or whatever has been 'socially constructed'. There are many different versions of these arguments concerning 'the social construction of *x*'[43], and those who argue in this way make different theoretical and explanatory claims for this approach. Let us consider social constructionism as it has been applied in laboratory ethnographies that demonstrate the crafting of facts and artefacts in science and technology. Knorr-Cetina (1983) writes that "the constructivist interpretation considers the products of science as first and foremost the result of (reflexive) fabrication" (119) – a fabrication that is contingent upon particular people, a particular space, time, institutional culture, set of norms, etc. She explains that many ('first wave') laboratory ethnographic studies that take a constructivist stance on scientific knowledge (led especially by Latour and Woolgar (1986 [1979])) have seen it as their task to (i) reject the 'correspondence theory' (the idea that scientific facts and law statements correspond to independent realities) and (ii) elaborate the complex and manifold social processes of constructing facts

[43] Hacking (1999) in *The Social Construction of What?* presents a long alphabetical list that includes, for instance, *x* as brotherhood, danger, homosexual culture, literacy, nature, technological systems, vital statistics and Zulu nationalism (1).

and artefacts in laboratories. The idea that the products of science exist 'out there' as an independent reality is problematic – 'facts' and artefacts only *become* what they are, in a way accessible to us, through processes of inscription, being made visible, being made measurable, becoming subjects for wider community discussion as well as objects for experimentation. As Sismondo (2010) succinctly summarizes, constructivism offers three important reminders about the nature of science and technology: they are *social*, *active* and *not themselves natural*.

Some take the social constructionist view of laboratory activities to be somehow 'anti-science'. However, it is important to clarify that this view does not require an anti-realist position, or one that denies inherent reality of scientific facts and artefacts – it simply necessitates that 'technical' and 'scientific' activities be treated as social phenomena. In his celebratory review of *Laboratory Life*, Hacking (1988) argues that although Latour and Woolgar's work is strongly anti-realist in some sense, upon closer inspection, it is a certain *kind* of irrealism and one that actually does afford some realism. Latour and Woolgar's (1986 [1979]) work is consistent with a belief in the existence of facts about the world and the reality of unobservable theoretical entities. The claims of Latour and Woolgar require only that such entities do not exist *until they are constructed*. Latour and Woolgar (1986 [1979]) offer "quite [a] different doctrine from that of the anti-realists who say that theories are only instruments to be used but not believed, or those who say that the aim of science is empirical adequacy, not truth" (Hacking 1988, 281). Hacking (ibid) continues,

> Latour and Woolgar report a world full of facts, but those facts are the historical product of 'microsociological processes.' There *is* a substance, TRH, secreted in minute amounts by the hypothalamus,

> and whose structure is that of a tripeptide, a string of three amino acids. That is a fact. But it became a fact. (281)

Above all, Hacking believes that what is most important about *Laboratory Life* is that its conclusions are arrived at through a detailed attention to the processes of scientific experiment, a site too often ignored by philosophers of science who are caught up in an ungrounded realist / anti-realist debate about scientific theories and entities.

Turning briefly to other developments on the constructionist argument in SSK, we can notice that the nature of the claims being made have been clarified, perhaps in an attempt to spare a continuation of some heated debates. The work of Bruno Latour and Michel Callon has been very significant here. Publications such as Latour (1983) and Callon and Latour (1992) move away from stronger social constructionist positions that seem to undermine the privileging of techno-scientific 'facts' and practices by revealing their many socially contingent factors. In their second (1986) edition of *Laboratory Life: The Construction of Scientific Facts*, Latour and Woolgar notably removed the word 'social' from the title of the 1979 original, *Laboratory Life: the Social Construction of Scientific Facts*. They argued that, in the aftermath of their original publication, a slew of social studies of science commentary that demonstrated the pervasiveness of "social" construction effectively "rendered "social" devoid of any meaning" (1986, 281). Hence they chose to delete the term altogether to avoid the impression that they were allocating causal powers to this 'social' domain. Further, Callon and Latour (1992) argue that a one-dimensional "tug-of-war" between an extreme "natural realist" position, at one end, and an extreme "social realist" position, at the other, cannot suffice.

As the field of SSK has grown, studies have presented a more intricate analysis of scientific knowledge production along multiple axes – mapping out complex relations between things, people and concepts in a performative, heterogeneous network, with all elements considered in the same terms ("generalized symmetry"). This approach was developed into the influential Actor-Network-Theory (ANT), a theory about how things, concepts and people come together, relate, perform and fall apart in a heterogeneous actor-network, whereby all elements ('things' included) have agency (Law and Hassard 1999; Latour 2005). A key contributor here was Pickering's (1993) focus on 'the mangle of practice': where 'things' (machines, instruments, etc.) have a material agency and that they, along with scientific knowledge, practices and human beings, exist in a constantly shifting "mangled" set of relationships, all under various cultural and local influences. While my own study does not take an 'actor network' approach, it certainly demonstrates that 'things' have 'agency' – or rather, as I prefer to think of it, that it is hard to produce results and artefacts in the laboratory, not least because the components that synthetic biologists try to create and bring into alignment often 'say no' to the attempts to make them work in particular ways.

In light of this discussion, it is now possible to outline the position on social constructionism that I will take in the remainder of the thesis. I believe, as Hacking does, that identifying instances of 'social construction', is not particularly important or intriguing. It is true that certain entities, facts, people, conditions, etc. are made up in a complex social matrix, but this neither exhausts the process, nor amounts to an explanation, far less a critique. More importantly,

one ought to ask, "what's the point of social constructionism" (Hacking 1999, 5)? Hacking writes, "what unites many of the claims [in arguments that take the form X is not inevitable; X is socially constructed] is an underlying aim to raise consciousness" (ibid, 6). Certainly, the ideas and biological entities that are discussed in the coming chapters are partly social constructs. However, I am not driven to 'raise consciousness' about this in the present work. My focus, rather, remains on providing a rich empirical story of knowledge and material production in a relatively new field, and conceptually framing that data in a way that remains close to the details. While it might be possible to describe this as a process of 'construction', I believe this would add little intelligibility to the richness of the empirical account.

There is one other important line of argument in recent STS work that has relevance to this thesis – the generation of hope and hype that comes hand-in-hand with the emergence of any 'new' biotechnology. I have already said that synthetic biology is associated with promises of eventually producing biofuels, cheap drugs, applications for bioremediation and more; equally prevalent are worrisome possible future scenarios around bioterrorism and accidental release of genetically engineered machines into nature. There is extensive STS literature (e.g. in Brown, Rappert and Webster's (2000) collection, *Contested Futures*) that focuses on how various actors in budding areas of techno-science use resources, political power and rhetoric (hopeful and frightening) to create a 'direction' or convince an audience (e.g. funding bodies or a potentially sceptical public audience) of 'what the future will bring' (ibid, 4). Those who write about the construction of predictive futures (e.g. Brown 2003; Hedgecoe 2004; Nightingale and Martin

2004) often argue for the need to question and destabilise the assemblages of metaphors, expectations, agendas and promises made by spokespeople of nascent technologies, because so often the prophecies of these narratives turn out unfulfilled, leaving great disappointment as well as wasted money, time and energy after hope and hype deflates. Moreover, they have suggested that contesting the construction of futures in the present is essential in making wise policy decisions, concerning choices about resource allocation and managing more realistic expectations. Calling for more agency, accountability and responsibility in the political economy of biotechnological expectations is essential; however, the cycle of creating hope, energy and promise around an emerging biotechnology in need of substantial funding is inevitable, as is, to some degree, disappointment when a technology does not deliver on its hoped for applications. In the closing chapters of this study (6 and 7), I briefly attend to the matter of how a promising, yet also risky, future vision is being constructed and managed in the present as synthetic biology emerges. Other studies are under way that examine 'future scenarios' of synthetic biology that share a number of similarities with parallel fields of biotechnological promise and risk – in an early and to some extent speculative technology such as synthetic biology, such possible futures are in flux, evolving through a number of challenges and selective pressures. At this point, one of the most valuable resources that can aid in constructing good governance structures for synthetic biology's future is to have a highly informed view of the present. This thesis, with its empirical grounding in observing the contemporary practices of key actors in the UK, aims to contribute to such a view.

Intervening science and 'taking a look'

As already discussed, Ian Hacking's view on social constructivism has had a significant impact on the position I take in this thesis. Let me turn to consider a few more of Hacking's concepts and arguments that have been particularly helpful. In *Representing and Intervening*, Hacking (1983) describes his position as a 'realist about entities and an anti-realist about theories'. This broadly describes the view I take towards the material I examine in this study. To appreciate the significance of this position, one needs to realise that one of Hacking's major complaints about contemporary philosophy of science lies in its tendency to get caught in idealist thinking, trapped in out-dated questions of epistemology that view scientific knowledge as a representation of nature. Such conceptions, he claims, are simply out of touch with the realities of practising science. Hacking (1983) argues that scholars must get away from thinking about the "reality of representation" and move towards "what affects us and what we can affect", found in attending to what goes on in scientific experimentation, interaction and creation (146). When one examines the practices of contemporary science – as laboratory ethnographies do – the researcher can comment on the epistemological and ontological questions embedded in experimental work. Hacking finds too that these sorts of investigation can sometimes offer resolution to long-standing realist / anti-realist debates in philosophy of science. In brief, Hacking (1983) argues:

- Science's two aims are theory (representation) and experiment (intervention) where theories aim to describe "how the world is" and experiment and technology "change the world" (31). Representation and intervention are obviously connected, each informing the other.

- Contemporary debates around scientific realism deal with theory, representation and truth. Hacking claims that these discussions are "illuminating but not decisive" and are "infected with intractable metaphysics"; he asserts that "there can be no final argument for or against realism at the level of representation" (31). However, in attending to intervention – such as spraying niobium balls with positrons – then anti-realism seems less plausible.
- "We shall count as real what we can use to intervene in the world to affect something else, or what the world can use to affect us" (146).

Why is this argument relevant here? Synthetic biology remains theoretical in many of its premises – for example, the notion that you can black box the details of biological parts, devices and systems, and work at each level in a separable, modular fashion. For now, there is good experimental reason to doubt such a claim. To the extent that my work is critical of synthetic biology, then, this often relates to its poorly supported theories – representations that often do not reflect the realities of intervention. Occasionally, however, building BioBrick-by-BioBrick yields something that intervenes and affects something real. In Chapter 5, the reader will see how the Cambridge team built biological systems that produced a range of colour pigments, systems that could be hooked up to other parts and systems, adding a colour output. In other words, the theory enabled them to produce something that 'worked', though whether this demonstrated the truth of the theory is open to question. Nonetheless, biological entities that intervene in the world are produced. This is why the position Hacking describes as 'realist

about entities and anti-realist about theories' position fits most closely the attitude I have taken in this study.

This thesis also links to Hacking's (2002) view of historical ontology. Historical ontology is about "the ways in which the possibilities for choice, and for being, arise in history"; it is "not to be practiced in terms of grand abstractions, but in terms of explicit formations in which we can constitute ourselves, formations whose trajectories can be plotted [closely], … or, at one remove, that can be traced more obscurely by larger organizing concepts such as objectivity or even facts themselves" (ibid, 23). When Hacking explains that laboratory ethnographies are part of historical ontology, he comments on the difficulty of labelling this type of study – part history (of the present), part anthropology, part sociology, part microsociology, part philosophy, part paraphilosophy, but none completely fitting as an accurate descriptor of what good laboratory ethnographies and historical ontology actually do; Hacking prefers to call this approach "taking a look" (ibid, 64).

I find it particularly appealing to brand this thesis as 'taking a look', or belonging to the larger field of 'historical ontology' because, as Hacking frames these approaches, they are at once broad and inclusive of many kinds of problems and methodologies, but at the same time, also situated in detailed investigations of how objects, ideas and ourselves are constituted. This work 'takes a look' in asking socio-philosophical questions in terms of the epistemology and ontology of synthetic biology (e.g. exploring how ideas and entities are made), while employing socio-anthropological methods. Specifically, this work aims to:

(i) Explore the *conditions that make a new field of knowledge and living material production possible* (at the levels of what goes on in laboratories, as well as at wider community and cultural levels of synthetic biology).

(ii) Attend to (i) not in 'grand abstraction', but through research that occurred in a discrete period of time, in which I was situated with the scientists, engineers, entities and organizations under study.

(iii) Ultimately serve as a point of departure: from close microsociological research, one might later ask questions of social and political significance in a more informed way. How might synthetic biology's forms of 'engineering life' affect larger societal understandings of biology and 'the living'?

Synthetic biology-specific literature[44]

Let us turn to a growing body of literature that focuses more *specifically on synthetic biology*, exploring social, ethical, regulatory and legal issues. Loosely categorised as concerning social and ethical matters, some works consider contested definitions of synthetic biology (O'Malley *et al.* 2008; Rabinow and Bennett 2008; Fox Keller 2009); others provide an overview of debates in the UK context (Balmer and Martin 2008; Lentzos 2009); still others address the role of social scientists in collaborating with synthetic biologists (Calvert and Martin 2009; Macilwain 2009; Schuurbiers and Fisher 2009); Molyneux-Hodgson and Meyer's (2009) article addresses the formation of communities in the EU and UK; other publications provide transcripts that recount lectures and conversations in

[44] This section covers recent literature that comments on social, ethical, regulatory and legal issues as they have broadly been categorized in relation to synthetic biology.

the field (Debate 2008; Lentzos *et al.* 2008). Interestingly, there have also been a number of articles on social and ethical aspects of synthetic biology coming out of *Nature*, *Science* and other notable scientific journals; these articles have been authored by writers specific to these journals, as well as social scientists, ethicists, natural scientists and engineers, and largely target a readership of biotechnology experts (e.g. Ferber 2004; Check 2005a; Church 2005; Tepfer 2005; Bugl 2007; Editorial 2007; Serano 2007; Parens, Johnston and Moses 2008; Alper 2009; Bennett *et al.* 2009; Cameron and Caplan 2009; Editorial 2009; Kaebnick 2009; Pauwels 2009; Schmidt *et al.* 2009; Yearley 2009). This growing body of work indicates the significant extent to which a discourse on social and ethical issues is embedded in relations among synthetic biologists, policy makers and humanities academics alike. Most of these works, however, seek to open questions for debate and are often not rooted in substantial fieldwork.

What appears to be the most ambitious social science collaboration with synthetic biologists so far has been underway since 2006 as part of the well-funded Synthetic Biology Engineering Research Centre, or SynBERC.[45] Breaking down the SynBERC initiative, it is oriented around four thrusts: Parts, Devices, Chassis and Human Practices, each with its own set of specific goals. Paul Rabinow used to lead the Human Practices category (though has since been replaced by Drew

[45] SynBERC brings together engineers, life scientists and humanities scholars from UC Berkeley, MIT, Harvard and UC San Francisco and is funded by the US National Science Foundation. SynBERC is one of the most significant institutions of this kind, claiming its "vision is to develop the foundational understanding and technologies to build biological components and assemble them into integrated systems to accomplish many particular tasks; to train a new cadre of engineers who will specialize in synthetic biology; and to educate the public about the benefits and potential risks of synthetic biology. In essence, we want to make biology easier to engineer" (www.synberc.org).

Endy, a popular figure in synthetic biology)[46] and points out that the particular naming of this "thrust" was coined in order to "differentiate the goals and strategies of this component from previous attempts to bring "science and society" together into one frame so as to anticipate and ameliorate science's "social consequences" – this is a 'post-ELSI'[47] project" (Rabinow 2009, 303-4). Rabinow continues, "[t]he task of Human Practices is to pose and repose the question of the ways in which synthetic biology is contributing or failing to contribute to the promised near future through its eventual input into medicine, security, energy, and the environment" (ibid, 304). Rabinow's team seeks to engage in "critical examination" and "genuine *collaboration*" with synthetic biology practitioners with whom they are partnered, in "a relationship designed to facilitate a *remediation* of the currently existing relations between *knowledge* and *care* in terms of mutual *flourishing*" (ibid, 304-5). These goals, according to Rabinow's research group, are to be met through "improved pedagogy" in collaboration, where pedagogy refers not merely to training, but is a reflective process of developing a "disposition to learn how one's practices and experiences form or deform one's existence and how the sciences, understood in the broadest terms, enrich or impoverish those dispositions" (ibid, 305). Without belabouring further, the reader likely appreciates that this version of human practices is a highly theoretical endeavour, with rather lofty goals – aiming to foster collaborations that

[46] No formal publications report a reason for this replacement but it has been remarked informally that some relationships between SynBERS's Human Practices scholars and those in the technical areas have had a difficult start. Certainly, the reality of developing non-hierarchical collaboration has been extremely challenging (if not unsuccessful, according to some points of view).

[47] Post-ELSI refers to a paradigm that distinguishes itself from the 'Ethical, Legal, and Social Issues' (ELSI) model associated with the Human Genome Project when such considerations generally occurred downstream of scientific developments; in post-ELSI projects, the evaluation of socio-ethical matters occurs in parallel with scientific practice, helping to shape its development.

affect the deep-seated moral character of those involved to work towards mutual flourishing and the betterment of humanity.

To have such aspirations, Rabinow's team rationalised that they would need to invent a new form of *equipment* – "a practice situated between the traditional terms of method and *technology*" – in order to explore the benefit of trying to form collaborative relations (305-6). According to Rabinow and Bennett (2008) in their most comprehensive publication that outlines "Designs for Human Practice", "[e]quipmental platforms are characterized by constantly available generality. Platforms are designed to function effectively in the reconstruction of specific problems, while being plausibly applicable to a range of analogous problems" (22-3). Rabinow and Bennett (2008) lay out extensive tables, categories, modules, connections, modes, methods and purposes in the elaborate equipmental platforms system that they employ; these reportedly problematic platforms, however, are not useful in this thesis.[48] Its overly complex and top-down theoretical structure, rife with ironic use of technical terminology and potentially idealised accounts of synthetic biology, aspects of this human practices agenda have already come under strong critique (Caudill 2009; Edmond and Mercer 2009; eliciting Rabinow, Bennett and Stravrianakis (2009) in response). My reasoning behind not making use of the Rabinow group's approach differs from previous critiques, but can be summarised as follows: (i) this research project began with relatively open and exploratory questions about what it means to design and build forms of synthetic life; (ii) the confines of an elaborately plotted theoretical system were therefore

[48] Rabinow and other members of the Human Practices thrust are open about several problems they've encountered in this collaborative venture, often arising from power differentials between those practising synthetic biology and social scientists (Rabinow and Bennett 2008; Rabinow 2009; also noted in discussions I've had with members of this research group).

not particularly useful in this kind of an investigation; and (iii) I have the freedom to pursue scholarly interest without the same level of commitment to high 'impact' outcomes (as in Rabinow's group). Moreover, the Human Practices endeavour explains that its task, influenced by Weber (1949, 68), is to explore not the "actual interconnections of things", but rather, "the conceptual interconnections of problems", hoping to "open up significant new points of view" in a general sense (Rabinow 2009, 307). This work, however, seeks to do more of the opposite: I map out the 'actual interconnections of things' – the practices, processes, ideologies, teachings and beliefs – in a segment of the synthetic biology community. Though there is conceptual and theoretical analysis of the empirical work, this thesis does not seek to do the sort of meta-level, general, platform-creating work of Rabinow group's.

A few additional policy documents and academic publications specific to synthetic biology ought to be mentioned. Concerning regulatory and governance matters, a number of references point to open questions and, on occasion, give a few recommendations: NEST 2005; Garfinkel *et al.* 2007; HSE 2007; POSTnote 2008; Schmidt 2008; Balmer and Martin 2008; Nuffield Report 2009; Royal Academy of Engineering 2009a, 2009b; Presidential Commission for the Study of Bioethical Issues 2010. The problem I find – and this is partly why I sweep over such documents and reference them in chart form (Figure IV) – is that, at this point, they are largely repetitive (naming the same major concerns and questions), quite general and don't provide much valuable insight for this work's purpose.

The work that explores how synthetic biology might navigate a potentially tricky intellectual property landscape, Kumar and Rai (2007), for instance, discusses what a bioscience *patent culture* might mean for this field; for at least the last five years, this topic has received significant attention, though little resolution. By way of background to the patenting issues in synthetic biology, the reader should know that there are already several broad patents held in synthetic biology, some by universities and governments, others by private firms (ibid). When broad patents cover foundational technologies, there is a real prospect of inhibiting innovation[49] (Kumar and Rai 2007; Rai and Boyle 2007). Perhaps equally important, narrower patents that protect individual biological parts might also cover foundational elements that could inhibit researchers from accessing basic building blocks for their work. Rai and Boyle (2007) outline major questions in developing IP frameworks for synthetic biology parts, devices and systems; furthermore, they warn that the history of proprietary issues in related fields (such as genetics and software) might come together in a "perfect storm" that could significantly impede the potential of this new technology (389).

Given this worry that synthetic biologists may find their line of work caught in a "patent thicket"[50], alternatives in "open source biology" have been popular, particularly among those involved in iGEM. The BioBricks Foundation (BBF), The Registry of Standard Biological Parts (The Registry) and iGEM are all linked; for the curious reader, a brief exploration of these organisations' websites illustrates how attempts have been made to balance a certain altruistic sharing of

[49] In synthetic biology, foundational patents exist that cover, for instance, use of cellular machinery for information processing tasks, mechanisms that modulate cellular pathways and methods to select optimal DNA-binding proteins.
[50] A tangle of intellectual property rights that hamper research progress (Shapiro 2001).

biological parts with IP frameworks that might also afford commercial development of products and applications (also see Endy and Grewal 2010). Additionally, it should be noted that the open source culture in synthetic biology is, to some extent, competing with private and highly patented ('closed') ventures such as those in a different school of synthetic biology, the J. Craig Venter Institute's approach of synthetic genomics.[51] A lengthy discussion of legal dilemmas and proposed frameworks in synthetic biology is certainly possible[52], though that would occupy another extensive project entirely; I shall not go into further detail. What will be important later in this thesis is not any particular resolution or IP framework, but rather the influence that discourses about both *open source sharing* and *desires to patent and commercialise* have on the iGEM culture.

Bachelard and Canguilhem

I now turn to some works of Gaston Bachelard and Georges Canguilhem that may seem remote to this emerging field of synthetic biology. Yet, concepts in Bachelard's and Canguilhem's works, in a French tradition of historical epistemology, have been particularly illuminating and have significantly shaped my thinking for this thesis. In their approaches to history and philosophy of science, these scholars provide a *critique of reason* through illustrating important episodes in science; they believe that the history of science is not a continuous development of reason, but a series of *discontinuous* breaks; and, there is a shared

[51] Scientists working at the J. C Venter Institute (JCVI) are well known for their tendencies to conceal information and patent innovations related to synthetic biology – this is referenced in several reports (listed in Figure IV). JCVI's website: http://www.jcvi.org/. It is worth noting that although Craig Venter is often portrayed as a 'bad guy', not sharing with the rest of the community (Marshall 2009), several other synthetic biologists wish to patent and profit from their innovations.
[52] A brief list of publications that have arisen regarding patenting in synthetic biology: Rai and Boyle 2007; Kumar and Rai 2007; Calvert 2008; Hope 2008; Henkel and Maurer 2009; Rai 2010.

emphasis on rejecting grand theories and normative claims in philosophy of science, in favour of attending to scientific rationality on *regional* terms (that is, trying to understand rationality in a way that is informed by real details in science, as opposed to enforcing philosophical norms onto science) (Gutting 1989).

In fact, and not surprisingly, some of the early laboratory ethnographies that I have described made reference to these approaches. In particular, Latour and Woolgar (1986 [1979]) draw on Bachelard's notion of 'phenomenotechnique' in their argument that "the artificial reality, which participants describe in terms of an objective entity, has in fact been constructed by the use of inscription devices" (64). As Hacking (1988) points out, much of Latour and Woolgar's (ibid) usage hangs on how terms like 'artificial reality' and 'constructed' are interpreted, and there is an ambiguity as to whether there is a relationship between 'being artificial' and 'being an objective entity'. I follow Hacking (ibid) here when he argues that,

> "Virtually none of the phenomena by which we elaborate, articulate and test theories exists, in a pure state, in nature, before we create them. I find this not merely consistent with scientific realism (about entities and phenomena as opposed to theories) but positively an argument for it." (285).

Importantly, Rheinberger (2005) points out, Bachelard himself seldom uses the term 'construction' preferring the alternative English translation as 'realization' – that is to say, making real. Scientific entities are not immediately given, but rather, they take shape and are made real gradually, in a complex socio-technical process. This is the way in which I follow Bachelard's concept of phenomenotechnique.

Furthermore, the Bachelardian notion of phenomenotechnique (also written as 'phenomenotechnology' or 'phenomeno-technology' in English translations) is a conception of how scientific thinking works. With a broader aim to challenge philosophers of science to re-evaluate their views in light of dramatic shifts in the physics and mathematics of his day (late 1920s to the 1950s), when quantum theory, non-Euclidian geometry and Einstein's theory of relativity were all examples of 'epistemological breaks' and genuinely novel thinking, Bachelard (1984) writes:

> A truly scientific phenomenology is therefore essentially a phenomeno-technology. … It takes its instruction from construction. Wonderworking reason designs its own miracles. Science conjures up a world, by means not of magic immanent in reality but of rational impulse immanent in mind. The first achievement of the scientific spirit was to create reason in the image of the world; modern science has moved on to the project of constructing a world in the image of reason. Scientific work makes rational entities real, in the full sense of the word. (13)[53]

According to Rheinberger (2005), phenomenotechnique is emphasized as the idea that *technology* is at the heart of scientific thinking and practice. Rheinberger quotes a passage from Bachelard on the subject of microphysics, describing how, through the phenomenotechnique, "new phenomena are not simply found, but invented, that is, thoroughly constructed"[54] (Bachelard [1931-32] 1970, 18-19, as

[53] At the time Bachelard was writing, philosophical debates about realism and rationality in science were, according to him, mostly constructed falsely by philosophers pre-occupied with projecting their ideologies onto science – whether it be a positivist view of science as a continually progressive effort or about scientific discovery as an endeavour that first finds natural truths and then comes to a theoretical position. For Bachelard, such views neglect what has actually gone on (and what still goes on) in markedly different developments of science and mathematics. For Bachelard to say that scientific thought firstly involved 'conjuring up a world' in mind, before anything could be made material or proven real, was quite unusual for his time.

[54] Where "construction" means something like "realization" and "instruction", whereby scientific objects are engaged agents in the knowledge production process (Rheinberger 2005, 320-1).

quoted in Rheinberger 2005, 315). Later in the paper, Rheinberger (2005) elaborates:

> [A]pplicability is built right into the core of modern sciences' concept formation. … Applied rationalism is thus technically implemented materialism. It is not the idea of science in search of application, but of a science that is taken and accepted as science *because* it moves in and has always existed in the realm of the applicable, because its very epistemological constitution has a technical dimension, because application is built into the very meaning of concepts and into the rules of concept formation, because the technical is built into the experimental phenomena…" (324)

To summarise, then, scientific work has invention, construction and technical applicability built-in at all stages – from 'dreaming up ideas' through to experiment and making real applications. In this work, I make use of this concept of phenomenotechnique particularly in describing the early stages of synthetic biology research, when specific projects are being 'conjured up in mind' before they are tried in wet laboratory practices. Using this concept in such a way serves as a reminder that technology and application do not merely come 'downstream' of scientific thinking – technology and application are active when the scientific imagination, *the dreaming up of ideas*, is just beginning. Chapter 3 articulates phenomenotechnique in operation in describing how groups of students 'conjure up' projects that exist firstly in the mind before teams can even conceive of experiments or making something real.

Under a general framework of writing a history of biological concepts that rejects the notion that science consists in discovering phenomena in a continually progressive way, Canguilhem explores the conceptual and historical value of *vitalism* – where I focus in considering his work. In very basic terms, the doctrine of vitalism says that biological systems are not reducible to the purely physical

and chemical (the mechanics); mechanism is vitalism's relative opposite. Canguilhem (2009) explains that when one considers vitalism in the history of science, three things are notable: (i) the '*vitality of vitalism*' – that is, despite the many divisions and oscillations of biological theories throughout history, vitalism has been returned to time after time; (ii) the '*fecundity of vitalism*' – that is, an ability to reproduce or measure the fitness of vitalism; and (iii) the '*character of honesty in vitalism*'. According to Canguilhem, the rebirths of vitalism translate "life's permanent distrust of the mechanization of life" – this historian of biology continually finds "life seeking to put mechanism back into its place within life" (Canguilhem 2009, 73). Canguilhem's fascination with vitalism is helpful to consider as an opposing movement to synthetic biology's vision that often appears to be the epitome of a reductionist view of living systems, wanting to remake life into 'engineerable', mechanical forms.

There are three additional concepts in Canguilhem's (2009) work that I find useful in thinking about how to challenge the synthetic biologists' view of the systems they are constructing: (i) the relation between *machine and organism*, (ii) the complexity of an organisms' survival in a *milieu*, and (iii) the idea that only life is capable of generating *monstrosity*. Though I do not intend to discuss details of historical examples that Canguilhem explores, for me, his work tends to highlight important themes through which I can question and analyse empirical findings of the synthetic biology world. For instance, I question to what extent the materials that synthetic biologists work with can be thought of as *machine* or as *organism* – this changes at different stages in a research project and with different challenges or accomplishments. The concept of a *milieu* (though not used explicitly) relates

to my discussions of biological complexity and, at a larger scale, can be thought of as a concept to describe the cultural intricacies in which this field is practiced. Finally, notions of *monstrosity and the monstrous* remind us why, for some, it is unsettling that synthetic biology seeks to design and construct new forms of life.

Conclusion

This chapter begun with a brief roadmap, indicating where in the thesis the reader will find answers to the particular research questions at hand. For the most part, however, I have provided a review of a wide range of important literature for this study. I have discussed themes from sociology of scientific knowledge, from selected laboratory studies and from the social constructivist school of thought; I have described various influences I've found in reading Ian Hacking, including my particular satisfaction if this work is thought of as 'taking a look'; I then explored a range of quite recent scholarship that centres on various social, ethical, regulatory and legal issues pertinent to synthetic biology; finally, I examined some helpful concepts from French philosophers Gaston Bachelard and Georges Canguilhem. While, in the body of the thesis, I have not made explicit reference to many of the authors discussed here, their arguments and their empirical analyses have informed the approach that I have taken, and as I have indicated in this Chapter, there are many resonances between my findings and those of previous studies. The main influences on the approach I have adopted in this study have been Hacking's (1983) 'realism about entities and anti-realism about theories', Bachelard's (1984) notion of 'phenomenotechnique' and Canguilhem's (2009) reflections on vitalism. In the core empirical chapters of this study, I have focussed directly on the analysis of the very large amount of empirical data

collected during my research. Rather than referring back to previous work, I decided to concentrate on providing a detailed account of a specific set of practitioners, places, activities and social dynamics arising in a fascinating field. Given the mounting academic, governmental and media interest in synthetic biology, I hope that such an empirical approach provides *basic research* (co-opting the typically scientific sense of the term) that may be *applied* in further questioning and different forms of scholarship from the social sciences.

2. FOLLOWING KNOWLEDGE AND MATERIAL PRODUCTION IN iGEM

Given that this thesis aims to unravel questions surrounding knowledge and material production in synthetic biology, as well as to investigate beliefs, hopes, practices, ideologies and tools of the field, I have taken a qualitative methodological approach. This chapter explains my entry into the field and how I used ethnographic techniques to follow a particular narrative. I also discuss how evolving relations with participants shaped the course of this study. Finally, I describe the kinds of data gathered and how I developed a methodology for a suitable analysis.

2.1 How to follow the narrative

In 2007, while working on my master's dissertations and starting to examine this field, there were only three or four UK laboratories doing what might be considered synthetic biology; however, I had a critical advantage in the form of a previous contact, Dr. Thomas Wiseman (pseudonym), a lecturer at University of Edinburgh who had taught me microbiology as an undergraduate. I contacted Thomas to ask whether he knew anything about synthetic biology and, as it happened, he was amongst the first of UK leaders in the field. From that initial key informer, a contact list grew as I sent emails, telephoned and networked at any synthetic biology event or conference I could attend; eventually, I had a good dozen or so relevant people to interview for my MSc research.

While at the University of Cambridge in 2008 interviewing two distinguished practitioners of synthetic biology, I had the opportunity to meet and talk with that

year's iGEM group. Though the iGEM perspective and competition was not a concentration in my MSc research, I was struck by how excited this group was to be part of 'the synthetic biology movement' and I began to think about the significance of inspiring and educating these students. Having had some experience speaking to established academics and equipped with a general knowledge of the workings in the community already, when it came to deciding my PhD focus, I knew that investigating the iGEM competition would be a rich site for social study. Furthermore, iGEM was a place of inquiry that – in early 2009 – was neglected by the steadily growing group of social scientists, ethicists, NGOs and policy makers that were examining and writing about the emergence of this potentially controversial biotechnology. Finally, I suspected that as a young researcher with an undergraduate background in biomedical sciences, I might have somewhat privileged access to be able to understand the science and be accepted by a group of undergraduate iGEMers.

And so begins the story of staking a place at two prestigious universities as the resident social scientist in groups of life scientists, engineers, physicists and computer scientists. Having made good contact with a few of the UK's main synthetic biology practitioners, access to the chosen field sites was relatively easy to acquire.[55] I had been informed well in advance that I was welcome to follow and participate in the Cambridge iGEM team; however, when I met with three leaders for the iGEM group in early May to discuss my research and formally obtain signatures on consent forms, a few conditions were placed on my proposal

[55] An institutional alliance between BIOS and Imperial College's synthetic biology group – in the form of the Centre for Synthetic Biology and Innovation (CSynBI) – also factored into rather straightforward access. Notably, however, I had already met and interviewed the key contacts at Imperial College prior to the formation of CSynBI, during my MSc research.

(see Appendix I). One of the head advisors – naturally with the interests of iGEM students in mind – was concerned about the extent to which I might reveal personal rifts within the team or faculty; he explained that he would not be happy if my work 'spiced it up' and strayed too far from 'what goes on in the science'. As delicately as possible, I talked further about my research interests and we laid out a few more agreements: for example, all students would have to consent individually and advisors could request to see my work to ensure its content did not sacrifice the professional or personal integrity of participants. I modified the agreements that were eventually signed by the involved faculty at Cambridge and later paid great attention to explaining the nature of my research to iGEMers, obtaining signed consent from each of them. At Imperial College, the case was more straightforward as I had been attending the synthetic biology undergraduate course since January, building rapport. Upon asking for access, a meeting was arranged and I outlined my research, then all the advisors signed consent forms, with the only minor added condition that I would 'not reveal the scientific content of the project until after the Jamboree'.[56] Again, I explained my research and had consent forms signed by all the students. With participant consent, a commitment to being open to questions, maintaining respectful relations among the actors in the study and using pseudonyms (where agreed) throughout this thesis, I have done my best to pursue this work in an ethically responsible manner.[57]

The coming chapters proceed with the backdrop of a chronological narrative, involving a set of characters whose roles, personalities, gender, goals, hierarchical

[56] This was 'due to IP reasons'. It is amusing that at one institution, the concern was about me straying from the science; while at the other, it was that I might reveal too much science and compromise the group's intellectual property.

[57] I don't claim that participants are fully anonymised as websites are given and it was agreed that institutional and disciplinary affiliations would be disclosed.

positions and institutional affiliations are relevant. A useful reference list of this work's main characters (with a description indicating participants' status and disciplinary affiliation) is provided prior to the Introduction (p. 8-9). Chapters 3 through 5 follow a trajectory of practices and processes in the two home laboratories as the teams brainstormed, decided on a project to pursue, navigated the challenges of engineering biology and eventually made a synthetic biological system (or part thereof) from late June to October 2009. For the sake of clarity, as well as for the integrity of what occurred in two quite different groups, these chapters are divided into two main sections, delineating the Cambridge and Imperial College teams. In Chapter 3, I briefly discuss how synthetic biology was taught at the respective institutions, as it was through participating in undergraduate courses that I (and most of the iGEMers) had the first technical point of entry into the field. At Cambridge, I participated in a two-week intensive crash course that took place directly before iGEM time began; it was the first year that this course was formally run and, in addition to all the iGEM students being present, there were a few other Cambridge undergraduates taking the course, four interested designers and me. At Imperial College, the synthetic biology course was a great deal more formal, running the full length of a term and getting stronger in its second year with a class of about twenty-five undergraduate engineers and life scientists. Attending both courses was useful in several ways: it provided a technical introduction to synthetic biology; it was a way for me to demonstrate 'seriousness' or 'commitment to the science' to the groups I was trying to work with; it showed me how synthetic biology was being taught, especially marked by enthusiasm and rhetoric that aimed to get students involved

in the discipline's development; and, it was a way to build relationships and trust that would afford me better participatory opportunities.

To give a sense of how I went about conducting my fieldwork, I will outline a few practicalities of my schedule. At first, I planned to spend full and alternating working weeks at each site, staying in a Cambridge college room so I could participate in evening activities. Obviously, access to the Imperial team and activities in London was an easy tube ride away. My alternating weeks between the sites worked out fine for a couple weeks and there were occasions for evening drinks and dinners as team members got to know one another; however, as time went on, the evening get-togethers faded out in Cambridge and that team developed a work pattern that generally consisted of weekday laboratory hours from 9 / 10am to 5 / 6pm (with occasional weekend workdays), where, for the most part, individuals' would return to their personal lives in the evenings. To save money and not spend lonely evenings writing field-notes and reading in a Cambridge dorm room, I decided that I would commute for the remainder of my research time. This actually became more advantageous when I realised that alternating between groups on a weekly basis left me quite out of the loop, missing five workdays in a row at a given site. So, when I began commuting to Cambridge, I also alternated between teams more frequently; typically, I spent three days a week at one site and two at the other, switching the balance weekly. My dozens of train journeys were devoted to writing field-notes or reading Wiki entries and other recommendations from participants. When both teams settled into a routine towards the end of July, I realised the need to allot myself an occasional full day of reflection and writing, necessary as it was to occasionally

re-focus when I felt 'lost' as a researcher in the field – not knowing what I was looking for exactly or how I would use all the data I was collecting. Alongside a group of iGEMers learning what it meant to become synthetic biologists, I too was learning what it meant to conduct ethnographic research.

Although Chapters 3 through 5 take place in the teams' UK laboratories and involve thick description in chronological time (answering how these groups imagined, designed and built synthetic biological machines), each chapter has a core analytic theme, influenced by literature discussed in Chapter 1. In Chapters 6 through 8, the narrative departs from the home laboratories and expands to describe what happened at the iGEM Jamboree's international stage; how iGEM is a tool for developing synthetic biology on a global scale; and finally, the reader arrives at a new space through which to consider synthetic biology's social and philosophical impacts in light of a real story that's been told.

2.2 Evolving relations in the field

According to Hammersley and Atkinson (1995), the two most important requirements of social research are fidelity to the subject under study and reflexivity as a researcher – it is essential that a good ethnographer has self-conscious awareness of what is learned in a given study, how it is learned and through what social relations. This work is embedded in the context of its production: as a young, female researcher coming from what was often seen by senior participants in the field as a 'soft discipline' (the social sciences as opposed to the real sciences), I was trying to penetrate a world where those at the top of the hierarchy were mostly well-established, male academic scientists and engineers.

One can appreciate that my role in elite synthetic biology circles would occasionally involve unfortunate dynamics – my age, gender, methodology and subject of study were all, at some times and by certain participants, viewed as points to undermine my purpose where I did not 'naturally' belong. Such undermining was thankfully rare and did not pose a significant threat to my work; aside from two or three people who were not particularly supportive of my research and occasionally made this known (or at least felt), I largely had good working relationships. I believe the fruitful interactions I developed are partly owed to two important features of the synthetic biology culture: (i) many ideals are based on embracing interdisciplinary views and tools (not only in science and engineering, but also extending to humanities and design) and (ii) the younger iGEM generation tends to be particularly excited by the alternative and diverse disciplinary associations of this field. It was nonetheless essential to this study's success that I continually reflect upon my role in the field, thinking about how I could open opportunities, forge good impressions and develop as a researcher. This section provides preliminary insight into how my interactions with participants developed over time.

At Cambridge

Cambridge and Imperial College have unique institutional cultures where different values and goals are relevant; hence, I consider examples from each site in turn and am careful about when to, and when to not, meld analyses.

I met Andy at a conference in early 2008, and he was my first point of contact with the Cambridge circle. Over the course of my master's and doctoral research,

Andy became the most important contact for me in both the UK and international synthetic biology communities, as he proved to be one of the most extraordinarily outgoing networkers and enthusiasts in the field. Andy was also a frequent source of insider gossip so long as I kept it off the record; though I do not disclose such sensitive information and cannot be sure of its accuracy anyway, learning insider politics over the odd informal coffee certainly added texture to my knowledge and directed some lines of inquiry. With good contacts in place (having met Samuel, Geoffrey, Frederick and Andy on several occasions) and relative assurance that I'd be welcome to participate in the crash course and summer iGEM programme, the real journey of evolving relations began.

After spending only a few intensive days in Cambridge, it was clear that a non-hierarchical and convivial atmosphere was being fostered in the group – a number of pleasant discussions (inclusive of students, supervisors, visiting designers and me) over tea breaks, lunches or the odd drink in a pub helped set this tone. Having sandwiches in large group circles with the sun beaming down on the immaculately groomed lawns of Downing or Emmanuel College became a very fond memory of the first two weeks when, in many ways, I was participating as other iGEM students were: taking in a mass of synthetic biology information, doing laboratory experiments and getting to know everyone. I was of course also an outsider,[58] 'the social scientist from LSE', often misperceived as the 'expert' on the whole range of 'social, ethical, political and legal challenges in synthetic biology'. This was an obviously overstated label to carry, and something I would occasionally try to shake by explaining to participants my interests in 'scientific epistemology' and

[58] Notably, in a somewhat similar way, the four visiting designers taking the course were also outsiders – non-Cambridge students and not scientists or engineers. Being part of a *group* of outsiders softened feelings of difference that a lone ethnographer typically feels.

'ontology'. However, it seemed clear that, at least initially, to perceive me as the person examining 'social and ethical stuff' was far more convenient. I accepted this perceived view on occasion, even using it to describe myself in the early days of fieldwork, as I felt (inevitably) uncertain about how my research might turn out. At some stage, I simply told myself to stop worrying about the label and carry on with the work at hand.

When the course was over and only the core group of iGEMers, advisors and myself remained,[59] a routine began to settle. Students were generally in the laboratory on normal workday schedules and I would arrive on my Cambridge days to observe and participate from about 10am to 5pm (and, when possible, would stay along for evening activities). On a typical day during the middle-period of the project (Chapters 4-5), students gathered in the morning to brief each other on who was doing what and gave updates; then, they would set to work, some in the wet laboratory, others working on computers to model reaction dynamics, research or add to their team Wiki. I would arrive at the laboratory, promptly set up my computer, notebook and camera, then get myself into rotation, jumping between individuals or small groups working on particular tasks: I learned about and carried out laboratory experiments; learned about computer modelling (though avoided actually doing this so as not to reveal great mathematical and computer deficiencies); took copious numbers of photographs; and talked with advisors. One of the running jokes in the group was that my role was to go around asking, 'what are you up to?' I was careful not to probe to the extent of annoyance and for the most part, I think I struck a good balance between

[59] The handful of non-iGEM undergraduates and the designers left after the two-week course.

asking questions and getting involved and also sitting back to observe, letting the scene unfold and giving everyone space. During particularly stressful times – often the result of failed experiments or a need to re-evaluate a given goal – I would sometimes sit with my laptop and take field-notes. For this kind of periodic retreat, I was eventually teased by one of the students: "Aren't ethnographers supposed to scribble down their notes in the bathroom or something?" At which point, it was also suggested that I should "do something", helping in an experiment. I was always happy to jump to those calls and became aware of my increasing integration as time went on.

To convey the developing friendly atmosphere in context, I'll share a memorable anecdote. In making their Wiki site, the Cambridge group added a 'Friends' of the team page, where one finds a blurb about the visiting designers and I.[60] The caption that the team endearingly wrote for me reads:

> **Caitlin Cockerton:** Caitlin is from the London School of Economics and is interested in the ethical implications of Synthetic Biology. She is also following the Imperial 2009 iGEM team, who she likes, but not as much as us.

This blurb entry and my continual back-and-forth between institutions led to a short flurry of Twitter exchanges between the Imperial and Cambridge teams, which bantered jokingly about who had more 'Caitlin time':

> **Cambridge (11am, 29 July):** Stop stealing Caitlin from us, she's ours!! ;D
>
> **Imperial (2:11pm, 30 July):** We found Caitlin crying after only 4 days in Cambridge.
>
> **Caitlin (2:23pm, 30 July):** Wonderful iGEMers… Please stop this sibling rivalry… I love you all equally.

[60] http://2009.igem.org/Team:Cambridge/Team.

Silly though these exchanges may be, they nonetheless signal that I was receiving informal embrace by the students. As the summer progressed, running jokes developed across all members of the very humorous Cambridge team, as students and advisors got to know each other; another tease I periodically received would occur in the midst of a laboratory mistake of some sort[61] or a dispute, when someone would typically say with a chuckle, 'Caitlin – you got this one *on record*?!'

My closeness with the team grew as we spent countless tea breaks and lunches together, witnessed each other's laboratory successes and failures and all developed as researchers. As time went on, students also took greater care in explaining to me what they were doing; they knew I was genuinely interested in the concepts, tools and techniques that they were using and would not dumb down their explanations for the social scientist (though having an undergraduate degree in biomedical sciences also came in handy). Admittedly, this sometimes meant I was the recipient of more technically detailed accounts than I could hope to understand, but those moments lost in translation were nonetheless enjoyable and valuable. I also spent a good deal of time chatting informally with all of the advisors as they dropped in daily to check on the students and give guidance. Without the stress of term-time teaching and given the advisors' keen support of iGEM in general as well as this particular group and project, I usually had a handful of quality conversations with these experts each week. We talked about the team's progress, the development of synthetic biology, dangers or fears circulating the field, notable laboratories and scientists as well as institutional

[61] For example, one student poured acetone into a £20K piece of equipment, nearly ruining it (luckily, it was rescued). Another student melted together a bunch of plastic plates by accidentally putting them under heat treatment.

politics. Further anecdotes in later chapters add colour to this outline; but, with brevity in mind, I provide only a few additional highlights to illustrate my experience of evolving dynamics with this team.

After introducing their work during the crash course, Daisy and James returned to Cambridge, running two additional workshops, and later, they attended the Jamboree. The importance of these workshops and general influence from these designers in engaging the students' imaginations, opening up discussion and shaking up the usual laboratory atmosphere, cannot be underestimated. In part, Chapters 5 and 6 explore the impact that design had with this group; but for now, suffice it to say that the design perspectives and workshop activities encouraged the team to think about possible futures that not only demanded they reflect on the utility and aesthetic aspects of possible synthetic biology applications, but also pushed the students to think about their work in a complex societal network. These workshops were also very fun – usually ending at a pub or with a group dinner – adding significance as real team bonding occasions.

Skipping forward to the iGEM Jamboree, the relationships I had with participants continued to get stronger; in fact, the significance of those four non-stop, incredibly demanding, exciting and emotional days cannot be underestimated (Chapter 6). In the lead-up to the Cambridge team's scheduled presentation, I spent a great deal of time with them, sat in packed and buzzy MIT auditoriums, listening to dozens of impressive teams show off their projects; I also tagged along to tour MIT and Boston / Cambridge, led by the well-connected Andy, who

had lived and worked there[62]. Finally, being in the same hotel as the Cambridge team, I shared moments of defusing: watching mindless television one evening, going to dinner, chatting over drinks and even going out dancing over the course of the weekend. I also had profound talks with advisors – conversations that reflected on the summer experience and looked forward to what would happen at the Jamboree and in the more distant future for the iGEMers. Then, when it came to the team's presentation day, I was with them as they put together last-minute preparations and managed their nerves and excitement; I sat in the full-house audience with the beamingly proud advisors and watched the group give a fabulous presentation. On the closing day of the Jamboree, I spent most of my time with the Cambridge group as one exhilarating moment followed another: they were announced as one of the six finalists; they presented their work again (as all finalists did); they won the Best Environmental Project prize; they won the entire competition (receiving the Grand Prize BioBrick Trophy, shaped like a giant Lego™ block); finally, when the competition ended, there was a flurry of congratulations to the team. Photographic opportunities and media attention ensued (including an interview with a journalist from The New York Times Magazine). These whirlwind four days were extremely important to the team and to my research. I suppose the last thing to mention here – in reflecting on evolving relations in the field – is that, by the time I flew back to London with the students, I felt I had truly become a friend of the Cambridge 2009 iGEM team.

A couple weeks following the Jamboree – after the dust settled – I conducted follow-up interviews with students and advisors, and was struck by how a number

[62] With the team, I saw The Registry, talked with iGEM founders and toured the important 'MIT syn bio crew hang-out spots' (the coffee shop, AI laboratory, roof garden, favourite pub, etc.).

of clips reflect participants' views of my role in the field. A small selection of such comments included:

- *One student said of having me around all summer:* "I think it was awesome – I mean anything that is going to integrate science and society is going to be really good. Otherwise, we can get kind of 'locked up' in the science bit! … It sort of made me feel more useful also… I felt that even if this whole iGEM thing failed and the project didn't work, it would have been useful for Caitlin's PhD!"
- *Another student, jokingly:* "At the beginning, you were like, 'I'm a social scientists and I'm going to be studying you and can you sign these release forms?' That was a bit weird! But then, once you'd been around a while, we chatted and we realized that you're fine!"
- *Towards the end of an interview with Frederick, he commented:* **"**I suppose going further into the future, you're actually in a rather good position now because you're one of the relatively few people who both considers the social side of things and actually knows a fair amount about the way iGEM, and the whole field of synthetic biology, works. I don't know where you see yourself going but presumably there ought to be plenty of job opportunities for you."
- *In conducting an interview I remarked that I at least felt that my presence with the students generated a "vague awareness" and interest in how synthetic biology fits into wider social contexts and research. Geoffrey replied:* "I don't agree that it's a '*vague awareness'*, because I think what people should be taking more on board is that although there are traditional ways of learning, those probably don't work in these contexts [in iGEM]. You can give a lecture on ethics, but basically the kids are just going to yawn, OK, and they won't learn anything. But when you talk about it in the context of what they're doing and you're asking them questions – it's insidious in a certain way – but actually that's the best way to learn and the best way to understand how the process works, by participating in it, not by being lectured at."

The relationships with participants at Cambridge grew stronger over time, and the perceptions of my work also changed – eventually, some participants took an interest in what I was doing, and the quality of exchanges I had with students and advisors about our respective research and future goals is something I am very grateful for. The informal conversations I had were invaluable, not least in developing a rich understanding of this field, and in particular of how iGEM

operates as a special tool to support the development of synthetic biology. My last proud moment took place in November – while helping to make a short film about the Cambridge iGEM project[63] – when Andy described my work to the film-maker as being about 'knowledge production in synthetic biology', not merely captured in a token phrase about 'social and ethical issues'. By the time I finished all the interviews and concluded my official time in the field, everyone at Cambridge expressed their best wishes to me, extended invites to return and requested updates and future works to read. I am deeply thankful for the learning experience I had with the Cambridge team and for the warmth that they extended to me.

At Imperial College

My start at Imperial College was fairly smooth, partly due to participating in the undergraduate course. However, only half of the iGEMers took the synthetic biology module and so my integration at that stage had more to do with gaining rapport with senior figures – lecturers such as Roger, Bernard and John, who were also iGEM advisors. As this was a formal course taught from January to April, there wasn't the intensity of full days with lunch breaks, extended tea time and post-work drinks as I had experienced at Cambridge; I simply showed up, took my place in the margins of the classroom or at the laboratory bench and tried to learn as much as I could. I talked with students and lecturers when possible, before and after class or in the occasional quick coffee break, but on the whole, the classroom group was quite serious and stuck to their social cliques (those in the Bioengineering faculty sat in one part of the classroom and those in Life

[63] http://vimeo.com/19759432.

Sciences sat in another). The students on this course were focused on getting good grades and, understandably, the academically rigorous atmosphere didn't afford me an opportunity to get close to anyone. Still, laying contact and knowledge foundations during the course led to a smooth transition to working with the iGEM group, which began in February with a series of iGEM try out meetings.

These try outs occurred after a pitch-style meeting organised by the advisors when they spoke to over 50 keen engineering and life science undergraduates about the wonders of synthetic biology and iGEM. This period is discussed in the next chapter, but it is important to mention how my role in the field began to take shape at that stage. During the try out meetings, I did not participate with the iGEM candidates (who were busy rehearsing their knowledge and presentation skills) and instead took mostly an observer view of the students, while also trying to participate in side conversations with advisors as they judged the group. A few advisors welcomed me with interest in the research – asking me questions, touring me around laboratories, meeting for coffee and generally helping to facilitate my early days at Imperial College. Most were rather neutral to my presence; however, there was one advisor who was initially forthright about his distaste for social studies of scientific communities, evidenced by his occasional laughter and snide comments.[64]

As the lead-up to selecting the iGEM team and planning the summer continued, I was almost always invited to the meetings, including ones that were only for the advisors; and yet, I had a distinct feeling that my presence at Imperial College

[64] I later discovered that Pierre had a certain cynicism about many topics, including research in his own field.

received mixed reception. I was also not alone in receiving a mixed welcome. A designer from the Royal College of Art was interested in working with the Imperial College iGEM team and proposed to run a workshop similar to the sessions that Daisy and James did at Cambridge. There was one meeting between three advisors, the designer and I, as well as a number of informal conversations, that revealed to me scepticism – oddly combined with interest and excitement – of interdisciplinary interactions with the humanities and design communities.

I proceeded to work at Imperial College without substantial difficulty; however, there was an occasional feeling of being the token sociologist[65], which contrasted with the more integrated culture at Cambridge. Moving forward in the trajectory of developing interactions, things changed significantly once the team was chosen and a routine was established. I 'hung out' with the iGEM students far more than with the advisors. When students and advisors met (especially when it was with senior advisors), my presence received little notice – all eyes were on the iGEMers while they worked to justify their ideas or experimental progress under the pressures and standards of their superiors. In Chapters 3 and 4, the reader will find that the Imperial College team struggled to pin down a solid project plan, but worked tirelessly in researching ideas well into July as stressful interactions between students and advisors ensued. During this period, I did a lot of sitting back, observing and not interfering. I always had lunch with students and shared coffee breaks in which my relationships with them became more relaxed and friendly; at the same time, my relationships with advisors was more remote.

[65] Although my entry into Imperial College's synthetic biology group was not officially organised through the alliance linking BIOS to CSynBI, because of what was then a recent joining of these institutions, I sometimes felt that my presence was merely viewed as the 'token' gesture of inviting social scientists into the laboratory as part of the institutional set-up.

One of the fascinating things that happened was that I became a confidante to a few members of the team while they were increasingly pushed and critiqued by advisors for having not made the progress that was expected of them (until finally, at the Jamboree, when the team did extremely well and were heavily praised). Part of the routine at Imperial College was for students to meet daily with at least one of the advisors (more often, the junior ones, Pierre, Max and Olivia) to give an update on progress and planned work, and to also meet weekly with a larger panel of the advisors (including at least some of the senior faculty, Roger, Bernard and John) for a presentation and feedback session. I was present for a number of these sessions and documented a few that were highly critical of the students' work; however, I was not always present (as I'd been in Cambridge), and would tend to get filled in on events I'd missed by the iGEMers. It was in such catching up on missed information over coffee breaks that I realised I was becoming closer with the group as students confided in me about perceived harsh critiques and tensions that they were experiencing with advisors.

I gradually grew a little closer to Pierre and Max as well – two junior advisors who spent a good deal of time with the team, responsible for keeping an eye on the students and reporting back to the senior figures. We talked about synthetic biology, the team's progress and various institutional politics. Interestingly, although Pierre had at first showed distaste for my work, over time, I established enough credibility with him to be worth talking to while he watched over the team. By the time students entered into their wet laboratory work in August, I felt that despite a few struggles, I had solid and friendly working relationships to

participate with the Imperial College team in a meaningful way. As with the other group, I tended to rotate among students who were either doing computer and research-based work or conducting laboratory experiments, asking routine questions: What are you up to? How does that work? Can you explain this to me? Naturally, a few students were more eager to talk than others and I tended to spend a little more time with them, some of whom would make excellent teachers.

Probably the most significant point of participation – and of impact in terms of my evolving interactions with the team – was my role in helping with a human practices side project. Quite early on, I introduced the idea that if the team wished to do something for what has been labelled as the human practices stream in iGEM, I would be happy to help with such work. I offered this help, in part because I thought it would be valuable for the students, but also as a gesture of thanks for having received access to Imperial College synthetic biology research for a number of months. I knew too that a human practices component was a recent addition to iGEM judging criteria.[66] I thought that helping students with an undertaking in this stream would be a win-win situation and although it did turn out that way eventually, difficulties were experienced along the way. These tensions play out in Chapters 4 through 6. At this point, it is only important to note that a good deal of change took place – in team members' views, my own approaches and in collective interactions – through the challenges of collaboration beyond the technicalities of building a biological machine.

[66] On the competition's website, it notes that Grand Prize winners are evaluated for, among many other important factors, a consideration of Human Practice issues such as safety, security, ethics, ownership, sharing and innovation; also, there is a special award given for 'Best Human Practices Advance' (http://2009.igem.org/Judging/Judging_Criteria).

2.3 Data at the desk

I have shown that it was through numerous informal conversations and having a lasting and close presence that I was able to build good working relationships, confidence and trust necessary to gain a place in the field as not only an observer, but also as a participant. The openness and extent of this study equipped me with data for thick description of the ways in which the teams brainstormed ideas, settled disagreements, carried out laboratory activities, dealt with hierarchical politics and learned about the workings of synthetic biology as an emerging technology with interesting socio-political dynamics. The final methodological issue I'd like to discuss concerns how I came to generate and interpret data from my multi-sited ethnographic research. Having completed almost a year of fieldwork in December 2009, by the time I had re-organised, printed photos and transcribed hours of interviews, I had a dozen rather large binders of field-notes, printed photographs, interview transcripts and media resources. These stacks of data felt rewarding but even more so, daunting.

I shall begin by outlining what I have done with the most straightforward data source: the interviews. At Cambridge and Imperial College, I conducted two sets of interviews with students, one during the middle of the projects and one after the Jamboree; I interviewed all the advisors at least once (except two at Imperial College, one who did not respond to repeated requests and the other who declined); I also conducted interviews with keynote synthetic biology figures from the US, as well as informally interviewed a handful of iGEM teams from around the world while at the Jamboree. Having to suit participants' busy schedules and meeting in sometimes less-than-ideal contexts, the interviews took on a variety

forms: they were conducted in quiet rooms, busy cafés, offices, hotel lobbies and foyers at MIT; they were sometimes conducted with just an individual interviewee and other times in small groups; they ranged from 30 minutes to two hours. These semi-structured interviews were recorded and transcribed, with a couple of minor exceptions[67]. To analyse the transcripts and develop core concepts in this work's substantive chapters, I use a number of established techniques: coding, writing memos, re-writing selected clips in categories and linking ideas through diagrammatic mapping. These techniques are written about extensively in qualitative research methods literature (Bulmer 1984; Strauss and Corbin 1998; Kvale 1996; Charmaz 2002; Flick 2002; Bryman 2004; Silverman 2005).

More complex, and deserving further description than the interview transcripts, are my field-notes. These became an amalgamation of three materials: (i) lecture slides and notes taken from attending synthetic biology courses; (ii) notes, presentations, protocols, diagrams and check-lists that were written by students and often posted on their work-in-progress Wiki's[68]; and (iii) the (more traditional) ethnographic field-notes where I wrote about daily observations and activities, described characters, settings and procedures, articulated how relationships were developing, as well as reported anecdotes. Materials of types (i) and (ii) were straightforward for me to access and use; however, writing and analysing ethnographic field-notes has (as expected) taken a great deal of time and energy.

[67] In one exception, an advisor at Imperial did not wish to be recorded in interview but I was permitted to take notes. Some interviews were selectively transcribed.
[68] http://2009.igem.org/Team:Cambridge; http://2009.igem.org/Team:Imperial_College_London; http://openwetware.org/wiki/IGEM:IMPERIAL/2009.

Sometimes there were independent research hours for students or repetition in laboratory practices. When this was the case, I would have some time during the workday to take jottings, if not more extensive field-notes, as well as participate and observe. There were, however, very full days too – packed with meetings, presentations and experiments while at the home laboratories, and then a non-stop pace at the Jamboree. There were several forms of field-notes from the empirical study – some entries are multiple pages of written prose, others are point-form notes, there are power-point presentations with additional notes and still others are audio-recordings (some loosely transcribed). Part of me wishes I was able to construct a more consistent set of data that could easily be read and understood by an outsider, but the results of this study inevitably reflect not only realities in the field, but also indicate my particular interests and choices to follow certain activities, agents, discussions, subject matters and dynamics more closely. According to many well-practiced ethnographers, though it is important for a researcher to strive for neutrality and elucidate a given subject matter in (as much as possible) its natural form, it is also essential that she demonstrate reflexivity and recognise that such research is always a somewhat personal affair (Hammersley and Atkinson 1995; Atkinson *et al*. 2001).

With the data at my desk, this work continued to be personal, as the more time I spent organising and analysing, I made connections and gained greater appreciation for where the most relevant material was located. Similar to the analysis of interview transcripts, when examining field-notes I used the above-mentioned popular techniques of qualitative research. I worked with my material as hard copies in ring-bound binders and did not use qualitative analysis software

packages; this meant that my piles of data were decorated in a personal style, with different colours of highlighting and various stickies representing themes or codes. I also coded in the margins with words or short phrases, such as 'blue sky', 'critique' or 'problem'; eventually, I categorised according to larger themes such as 'dreaming up ideas' or 'making real' (hence, data to be used in given chapters) and re-grouped excerpts from field-notes and interviews into new documents. Although I began coding and drawing out themes in the field-notes during my fieldwork, the coding, re-reading, writing and analysing continued throughout write-up stages – it has been a labour of building my thinking and analysis, layer upon layer, gradually coming to theorise more broadly about the detail. I have also benefited greatly from conversations with my supervisors that helped me strategically find ways into a rather large stack of data for a given section of writing; their expertise and comprehensive viewpoints alerted me to the need to step back when I felt 'too close' to the research material (as I often found myself thinking 'there's just so much to say!').

Finally, I turn to the visual data – the unexpected yet extremely valuable resource of over a thousand photos that show practices, thought processes and events during the two teams' journeys. The matter of visualization in science has been addressed by many in STS – for example, Latour (1990), with his concept of 'immutable mobiles'[69] and Suchman and Trigg (1993), in their examination of AI scientists working together on a whiteboard. I take a somewhat different approach, one that is a more pragmatic and particular one.

[69] That is, the argument that through the use of numbers, diagrams, charts and so forth, scientific practices create 'inscriptions' that bring together diverse elements in a two dimensional, stable and mobile 'immutable' artifact, that is 'mobile' in the sense that it can be moved from place to place, compared and amalgamated with other artifacts and made the object of scientific analysis in a 'centre of calculation' (Latour 1990).

I worked with this data in hard copy and electronically. I've taken inspiration from literature that may be classified under the umbrella of 'visual culture' (for example, Hall 1997; Evans and Hall 1999; Rose 2001), but have found that in developing a methodology to think about and use these photos, the most effective activity for me has been to talk with colleagues, my supervisors and participants from the field. I employed two broad categories for my visuals: (i) photographic field-notes and (ii) photos of 'mind maps' (or close variations thereof). In the first type, images generally capture *a scene* (e.g. in the laboratory, during a workshop or at the competition); images of the second type show *how students represented thoughts* on paper or on white boards (notes, diagrams, mind maps, doodles, etc.), on computer programmes and in presentations. Some images fall under both categories, but nonetheless this division was a helpful starting point of organisation.

With two major categories of photos, I began thinking about the sorts of questions I could ask of each kind. From the photographic field-notes, I stimulated my memory, supplemented and crosschecked with written field-notes and found answers to questions of this sort: Who is present in a given scene? When was the image taken? Where was the image taken? What were the details of a scene's appearance? What artefacts are present – tools, biological entities, lab coats, machines, suitcases, etc.? What do people's expressions convey? What is the nature of the activities that people were carrying out (precise, crude, silly, mind-numbingly repetitive, nerve-wracking)? Does the image capture something iconic in synthetic biology (as a few images in Chapter 6 do)? If an image is particularly

symbolic, how is it so? On the other hand, in images that portray ways of thinking (Chapters 3 and 4), such as mind maps, I ask questions like: What does the image's content capture (e.g. To Do list, protocol, goal, idea, collection of ideas)? Is the image largely diagrammatic or does it have a written explanation? How simple or complex is the mind map? How is the image's content used (in teaching, presentation, thinking through a problem, organisation), and by whom (for an individual or for many)? Who authored a given mind map and what does it say about how he or she was thinking (e.g. does it reflect their leadership role or disciplinary viewpoint)? These questions give flavour to the richness I found in the visuals – data that is highly relevant to this thesis, bringing the reader closer to the story than can be offered by description alone.

After days spent organising the electronic photo library, asking myself about what each picture revealed, writing notes and coding (attaching themes and stickies), I selected favourites that could potentially go into specific chapters. I began by considering 20 to 40 photos for each of Chapters 3 through 6. These favourites were sometimes supplemented with recorded discussions that I had with participants to clarify and discuss the contents and meanings in these photos. Finally, this personalised, step-wise method led me to limit the use of photos in a given chapter to only what is most helpful in illuminating important points.

Conclusion

This chapter has explained my entry into, and suitability to, this particular field study. I have also outlined the trajectory that the narrative follows and addressed

ethics of research (noting that, to the degree possible in this particular study, I have tried to anonymise most participants with pseudonyms; copies of the information sheet, consent form and further agreement for participants are also provided in Appendix I). I discussed the reflexivity demanded for this work and illustrated how I was integrated into this project, with my particular viewpoint, interests and experience of evolving relations with participants. Finally, I have outlined my methodological practices in generating and analysing data and discussed some challenges faced.

For an ethnographic study to address judgement for its validity, reliability and relevance, a researcher's best defence is to provide strong evidence of "data-source triangulation" in comparing different data sources that relate to the same phenomenon (Hammersley and Atkinson 1995, 230). In the coming chapters, the reader finds empirically dense work that draws its illustrations from field-notes, interview clips and photographs – my triangulation technique is clear. Although I have found sorting through this information pool a "messy affair" (Strauss and Corbin 1990, 31), it has equipped me with material to richly answer this work's core research questions.

3. DREAMING UP IDEAS

The Bachelardian (1984) notion of phenomenotechnique is at this chapter's core – the idea that, especially in generating breakthroughs, the scientific spirit must first creatively 'conjure up a world' in the mind before there is a chance of ideas being made material or proven real. This concept also emphasises that applicability and technology are built into all stages of scientific thinking and practice – even from the very beginning. Highly imaginative and application-driven brainstorming was the first major challenge faced by students in this competition and is the subject of this chapter. I show how students are encouraged to 'think outside the box' and come up with a range of useful (at least hypothetically) synthetic biological systems. (It is, however, important to keep in mind too another mode of science on-the-ground, one where much of everyday thinking and practice consists in a routine following of protocols and checking for results that are often elusive. This 'everyday' mode of scientific practice, I believe, can sometimes look as though it has forgotten the plot of phenomenotechnique. Interesting as this aside may be, it remains tangential to the driving point of this chapter.)

How do pioneers in synthetic biology come up with their ideas for the kinds of living machines they want to construct? This has been a curiosity of mine since I began learning about some of the popular work in the field. Well respected laboratories housing keen iGEMers have engineered bacteria to smell like wintergreen and bananas; they have made plates of bacteria act like photographic films; they have made cells 'blink'; they have also worked on cell-free systems to detect pathogens living on catheters, which often causes urinary tract infections;

they have engineered bacteria to produce haemoglobin that could theoretically replace red blood cells in transfusions; they have attempted to pump out biofuel from redesigned microorganisms; and they have worked on the development of biosensors that detect arsenic in drinking water. I wondered before starting this project, who had been dreaming up such ideas – sometimes wacky and playful, sometimes with a 'save the world' aspiration – and how were they inspired?

This chapter demonstrates how iGEMers were taught and encouraged to think along synthetic biology lines – for most of them, a new and different intellectual exercise. I then illustrate the kinds of projects that were dreamed up by each team until they decided upon their sticking idea and show how this was an activity not just of abstract thinking, but one that involved the use of 'intellectual technologies' (Miller and Rose 1990). That is to say, each team used certain *tools for thinking* – mind mapping, drawing pictures, making lists, setting up online discussion forums, presenting in certain patterns, etc. – that helped make, shape and develop ideas.

3.1 Dreaming up ideas at Cambridge

A crash course in synthetic biology

> Scientists discover the world that exists; engineers create the world that never was.
> – Theodore von Karman, engineer and physicist

This quote appears on the first slide in the introductory lecture of a two-week intensive synthetic biology crash course at Cambridge[70] and it immediately relayed an exciting message: by learning to engineer biology, students can help

[70] This course taught 12 undergraduates (plus four designers and me) synthetic biology basics; five out of 12 attended to receive course credit and they left after two-weeks, while seven students carried on after the course to pursue the full iGEM project. I only follow the iGEMers in detail.

create a new world. The reader will soon appreciate that the dreaming up of new ideas in synthetic biology is actually quite a challenge; however, many (not all) instructors believe that *students of synthetic biology must firstly be inspired by the creative potential of the field, before they execute the difficult and patience-trying work of actually constructing (or, attempting to construct) a functioning microbiological system.* Stirring creativity and intrigue about seemingly vast possibilities in 'building with biology' is at the heart of the Cambridge group's approach to teaching this subject. When Geoffrey was faced with introducing a class of science and engineering undergraduates to synthetic biology, all cramped into a poorly lit classroom on a sunny summer's day, his lecture was full of motivating highlights. A few details from this crash course (before focusing on the dreaming up of ideas by the iGEMers) will allow the reader insight into what these students' first taste of synthetic biology was like and also give background to some of the technical material that arises throughout this thesis.

The second slide in Geoffrey's lecture posed the iGEM questions: "Can simple biological systems be built from standard interchangeable parts and operated in living cells? Or, is biology so complex that each case is unique?" A working definition was then shown: synthetic biology is "the design and construction of new biological parts, devices and systems; [and] the re-design of existing, natural biological systems for useful purposes".[71] Another slide was divided into two pictures with the heading "Construction through Standard Interchangeable Parts": one picture had individual Lego™ pieces categorised under structural, motor, sensor, controller and internal logic groupings; the other picture showed a couple

[71] http://syntheticbiology.org/.

of assembled Lego™ robots, apparently in action. The following slide read, "Microorganisms as Genetic Machines", and it labelled parts of a bacterial cell as having environmental sensors, protein and chemical synthesis machinery, internal logic, communication mechanisms and motility. The desirable – though mostly fallacious – analogy that biology can be thought of as discrete parts that snap together like Lego™ to build a functional system was made clear in the first minute of the lecture.

This lesson continued to demonstrate ideologies and principles in synthetic biology. Another oft-cited timeline was illustrated, comparing the development of the electronics industry to the development of DNA technologies. The suggestion was that with accumulating discoveries and inventions over the last few decades[72] – plus the improving capacities in DNA sequencing and synthesis, and computer modelling of biological systems for 'in silico' design – synthetic biology looks to be primed for a path of exciting industry-scale development. Problems aside, I include this detail to show that these comparative histories are used to persuade students (and others) of a (possibly) prosperous future for those who get on the synthetic biology bandwagon. However, the Cambridge advisors in particular, among the accounts I have heard, are generally far more careful in making such comparisons and trying not to perpetuate future visions of the field in too hyperbolic a way. Indeed, Geoffrey qualified that doing a comparative history can only indicate a hopeful line of development for synthetic biology: "Are the supporting technologies sufficiently mature that we can move biological

[72] Citing Watson, Crick and Franklin's discovery of the structure of the DNA helix in 1953; Cohen and Boyer's invention of recombinant DNA technology (cutting and pasting sequences of DNA) in 1972; Sanger's sequencing of the first genome (phage 174) in 1975; Mullis' invention of the revolutionary PCR machine (used to amplify sequences of DNA) in 1983.

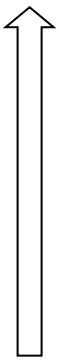
engineering from a simple bespoke process to a true engineering discipline? Well, the jury is still out."

Geoffrey continued elaborating a transition between what he called "First Generation Biotech", based on technologies such as PCR and recombinant DNA, and "Second Generation Biotech", of which synthetic biology is a part. In the first generation paradigm, he claimed, 'the majority of biological research focused on the study and analysis of naturally evolved systems' and there has also been 'ad-hoc construction of genetically engineered solutions', such as insulin production in bacteria and creating pesticide-resistance in crops. In the second generation, however, not only do practitioners in this line of work use first generation technologies, they also use far more DNA sequencing and synthesis, computational modelling and design.[73] Furthermore, it is the application of "engineering principles" that Geoffrey believes is key to rational design and construction of synthetic biology systems that can be made repeatedly, reliably and ultimately on a large-scale:

- **Modularity:** Genetic sequences for use in synthetic biology are broken down into separate, well-characterised modules such that they are easily inter-changeable.
- **Standardisation:** The application of uniform standards in synthetic biology will mean that the community of researchers can work with off-the-shelf standardised components, enabling predictable performance of parts, devices and systems under construction.

[73] Through informal conversations with synthetic biologists, I've observed that the meaning of *design* in synthetic biology remains contested, meaning different things to different people.

- **Abstraction:** The ability to insulate only relevant characteristics at a given abstraction level from the overwhelming detail of other levels (lower in the hierarchy) in a biological system will enable synthetic biologists to black box components and afford ease of use and construction. The abstraction hierarchy in synthetic biology is as follows:



  - **Applications** (e.g. biosensor, biofuel, biomaterial)
  - **Systems** (e.g. input – sensor – processor – output)
  - **Devices** (e.g. input, logic gate, output)
  - **Parts** (e.g. BioBricks of a particular type such as a promoter, a ribosome binding site (RBS), a coding region, a terminator)
  - **DNA** (the underlying genetic code – ATGCTTACCG…)
- **Decoupling:** Rules that insulate the design process from the details of fabrication will enable teams of parts designers, device designers and system designers to work together without having to know the details of each other's work.

Geoffrey continued, 'in order to develop an industry, an engineering discipline based on parts must develop catalogues and suppliers of those parts'. Again, there is a desirable analogy: for iGEM-involved and other academic synthetic biologists, they would like The Registry of Standard Biological Parts to model itself upon The TTL (transistor-transistor logic) Data Book. The TTL Data Book, I'm told, is *the* manual for design and construction of TTL digital circuits – for professionals and hobbyists alike. On The Registry website, one not only finds a catalogue of thousands of parts, there are also protocols such as Standard

Assembly of BioBricks, with its seemingly easy (though deceptively so) instructions for 'sticking parts together' via commonly used microbiology laboratory practices.[74] Supporting the large annual intake of iGEM teams by sending off BioBrick kits freely and receiving new BioBricks constructed, The Registry is continually growing in size and trying its best to maintain uniform standards (though this remains next to impossible in practice).[75]

The purpose here is to sketch the introduction to synthetic biology the iGEMers were given before they were challenged to think up their own ideas, so, I will not go through the 20-odd lectures; however, it is still worthwhile to provide a list of the other major topics covered (before discussing the laboratory practical sessions):

- Working with Genetically Modified Organisms (GMOs): risks and ethics[76];
- Visualising gene expression and cellular architecture;
- Use of fluorescence microscopy and 3-D imaging techniques;
- Metabolic functions in various strains of bacteria;
- Bacteria understood as machines that act as biosensors, biocatalytic systems, bioremediators, inhibitors and producers of materials and chemicals;

[74] http://partsregistry.org/Assembly:Standard_assembly.
[75] In 2004, iGEM teams submitted about 50 BioBricks to The Registry; in 2005, this number increased to about 125 parts; in 2006, it was about 724; in 2007, it was about 800; in 2008, it was 1387 parts; in 2009, it was 1348 parts (http://2010.igem.org/Previous_iGEM_Competitions). As one might imagine, it is very challenging for an open source registry used by undergraduates worldwide to keep track of the contents, ensuring that BioBricks adhere to standards and *actually function* as documented.
[76] The emphasis on safety, a key concern around synthetic biology in general, was evident. Topics covered included: dual-use dilemma; insufficient detection, analysis and response of potential biohazards; limited control of information databases and DNA synthesis companies; regulations at institutional, national and international levels; professional training in biosafety; and different classes of biological research / facilities (biosafety levels 1 to 4).

- How cell-level and population-level communication systems work;
- DNA sequencing and synthesis technology;
- How essential microbiology equipment works (e.g. PCR machine, plate reader, 'the robot');
- Mathematical modelling of biological systems;
- Computational modelling of biological systems and an introduction to programming languages for use in synthetic biology[77];
- Experimental design, organisational practices and using internet sites to document and share work (e.g. Wiki's and OpenWetWare);
- Synthetic biology applications and the makings of industrial-scale technologies (laden with analogies[78]).

Finally, the laboratory sessions that took up at least a few hours each afternoon were very important to the teaching style at Cambridge – it was in these practicals that students worked together and, for some, had their first hands-on experience of microbiology experiments. Many practicals were designed to showcase the toy-like systems that have been constructed, a few of them taken directly from old iGEM projects. The MIT iGEM project from 2006, 'Eau d'coli', was demonstrated by one of the instructors and everyone in class did 'the smell test', deciding whether a number of blind samples smelt like bananas, wintergreen or simply the normal foul bacteria smell; it turned out that our noses matched the

[77] Given by an expert from Microsoft who collaborates with Samuel and Andy, this interactive lecture taught the basics of a programming language that can be used to do 'in silico' modelling of biological reaction kinetics, 'predator-prey' systems, the catalysis of DNA and the workings of logic gates that operate inside cells. Working 'in silico' is meant to improve design of 'wet laboratory' experiments.

[78] The lecture given by Geoffrey and Samuel entitled, "The Industrial Revolution: based on innovations in coal, iron, steam and mechanical engineering," was full of comparisons about other industry successes that have been based on standard, interchangeable parts that allowed continuous production methods. Standards on nuts and bolts, as well as standards on mechanical and electrical interfaces were discussed. The emphasis on the importance of engineering standards cannot be underestimated.

correct genetic logic 60 to 90 per cent of the time. The class also carried out experiments that used colourful purple bacteria, photographic biofilms and imaging technology from Samuel's laboratory to visualise fluorescing microbes.

In addition to the microbiology experiments, there were a few unconventional sessions, designed to get students to work together and think about design, modularity, time-management, presentation and pitching. For example, the first day's practical was a team building exercise in which the class was divided into groups of three or four and challenged to construct a weight-bearing tower as high and as strong as possible in 30 minutes from plastic straws, tape, rubber bands and two plastic cups.[79] The class also had an afternoon to play with Arduino kits.[80] Basic Arduino kits can receive input from a variety of sensors as well as interact with computer software; depending on how one plays with Arduino, one can make a light show, construct circuits, play sound, operate robots and even hook it up to living cells. Finally, on the last day of the course, everything was wrapped up in a future-oriented Dragons' Den[81] competition where small teams had to think of a synthetic biology application and business plan to pitch to a board of external heavy-weight figures from across University of Cambridge as well as someone from a biotech start-up company. Students came up with a variety of imaginative ideas and found the exercise challenging and fun. The importance of building these alternative sessions into the programme, complementing an already

[79] This exercise was meant to get groups to first thoughtfully design what they would build, then to delegate tasks appropriately. Some teams built tall and architecturally sound towers, able to hold an impressive weight. My team didn't really grasp the idea of planning a good design ahead of time; our design 'evolved' after too much time wasting and unsurprisingly, during the weight-bearing tests, our tower crumbled. We decided that what we had built resembled a dead fish.

[80] "Arduino is an open-source electronics prototyping platform based on flexible, easy-to-use hardware and software. It's intended for artists, designers, hobbyists, and anyone interested in creating interactive objects or environments" (http://www.arduino.cc/).

[81] Modelled on the popular BBC television show (http://www.bbc.co.uk/dragonsden/about/).

'cool' set of microbiology experiments (compared to what one does in conventional biology courses), cannot be underestimated. Speaking to advisors about how they designed the course, Andy remarked:

> With the practicals, we tried not just to show off the systems but also leave a little bit of flexibility for the enquiring minds, a bit of inspiration and a bit of creativity, and I hope you noticed that a lot of the practicals weren't just 'do this set of instructions'… It was more about, 'here's a pallet, here's a tool, here's some fun, go do it, go think for yourself and come up with something you could do!'

Similarly, Samuel commented:

> In most university biology courses, we teach by exposition, except now it's PowerPoint slides and practicals following recipes. Then of course iGEM is the antidote to that because it's the opposite – it is exploration…
>
> It is team-based, so we don't try to isolate anyone but rather show that the students can draw on other people's expertise… And you've got things like the Arduino stuff that we did… which was demonstrating the idea of putting something together from modular components…

Returning to the quote that opened this section – "Scientists discover the world that exists; Engineers create the world that never was" – it was clear to me that the crash course not only equipped iGEMers with the basic synthetic biology knowledge they would need for the tasks at hand, more importantly, it provoked excitement and creativity. Tobey, a first-year engineer, told me later about how the crash course inspired him:

> I only heard about iGEM and synthetic biology just a month before starting all this. What appealed to me was that it is a whole new field of engineering and I think that is the most interesting thing about engineering – the big breakthrough's, the start-up companies… I don't want to go into anything too established – the appeal is about new frontiers…
>
> I've been in some group projects before but this is really original. Within the small team, you have the biologists that are really different in the way they think than to the engineers. And, without one or the other, we wouldn't have got anywhere near as far – and that includes physicists. And having you guys [the designers and me] from all

> different places and with all different interests – it was really exciting – especially in that two-week intro course because it was like we really were right on the forefront of this new field and we were all investigating it for different reasons…

Filled with a palpable sense of wonder after the crash course, the seven iGEMers returned to the laboratory the following Monday morning and faced one of the most challenging stages of their summer – they faced a blank page and had to come up with a great idea.

From blank slate to an idea that sticks

On the team's official first day, the iGEMers, their advisors and I all gathered for a quick morning briefing. The students were reminded of resources at hand – computers (to survey literature and previous iGEM projects), the library, a binder 'bible' of key synthetic biology publications, the staff's expertise and, perhaps most importantly, markers, stacks of large sheets of paper and a white board – and then the group was set to the task of coming up with some feasible, yet exciting, project pitches to present to the faculty in a few days time. After the briefing, aside from periodic visits from advisors to monitor progress and answer questions, the students were left largely to their own devices. The group promptly set to work and agreed that the best strategy would be for everyone to break off individually and research areas of interest, each with the goal of bringing at least one idea to discuss at tea break. Stationed along the laboratory benches – but with nothing 'wet'[82] in sight – the students began their "thought shower" (as Eleonore called it).

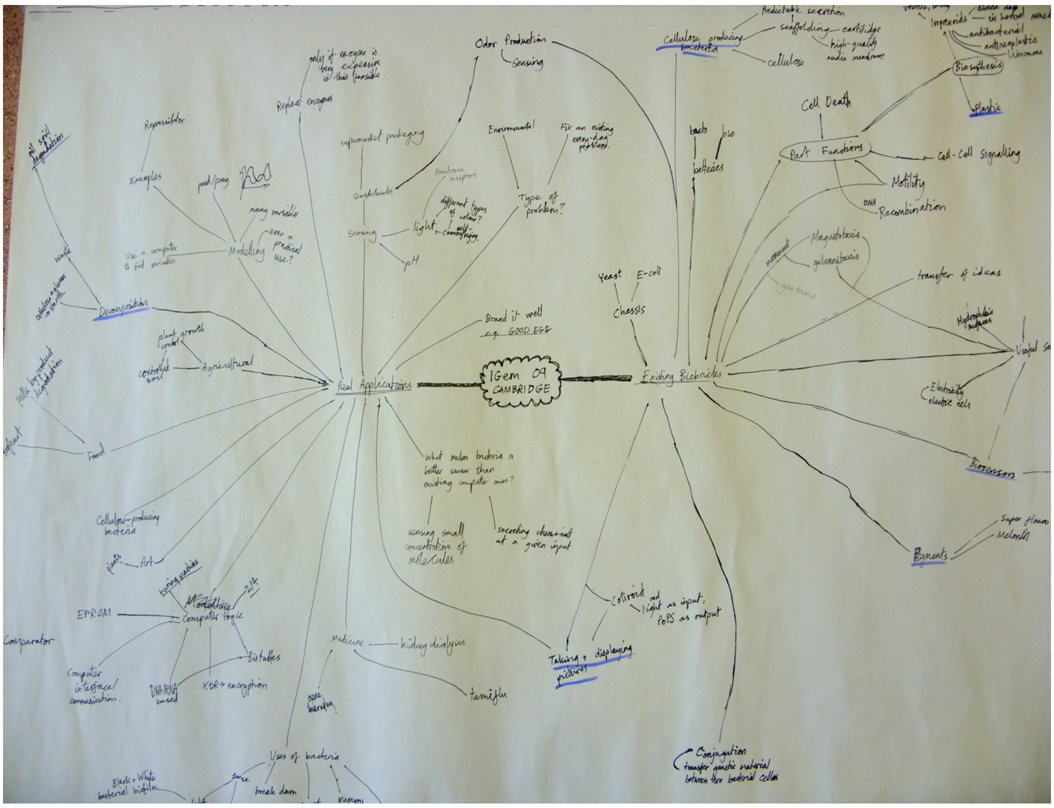
[82] See Key terms, 'wet lab' and 'dry lab', p. 11.

The first mind map (Figure 3.1) to discuss was drawn throughout that day – before and after the all-important tea time discussion– and was done by Tobey, an extremely curious engineering student who later commented:

> My favourite part of the whole thing was the brainstorming. Even though everything gets rejected right at the beginning, it is the most exciting part because you are thinking of all the things that could really be done… It is most creative at the beginning and, after that, there is still creative work, but it is sort of more routine – pipetting and stuff…

In Tobey's particular thought experiment, his diagram shows the large range of possible areas for consideration in generating a project idea – this was the group's major *overview* mind map. Notice that the diagram originated from the team's not yet existent project idea sitting in a cloud in the middle of the mind map, reading "iGEM 09 CAMBRIDGE", sandwiched between "Real Applications" and "Existing Biobricks".

Figure 3.1: Day 1 mind map



What stems from the "real applications" arm on the diagram's left, a number of branches illustrate biases towards what was learned in the crash course as well as Tobey's engineering background. Given (key advisor) Samuel's expertise in plant biotechnology, some students pushed their brainstorming in that direction too. Looking at the diagram, one can see an indication of this: the "agricultural" arm branches out to two linked thoughts, "plant growth control" and "controlled soil"; one of two major "type of problem" ideas is "environmental"; the branch off "art" is "plants"; "food", "sensing" and "cellulose producing bacteria" branches may all point to an agro-biotechnology bias too. By contrast, the branch for "medicine" only includes three ideas, none of which are elaborated – kidney dialysis, tamiflu and gene therapy – presumably a less developed area as the advisors had emphasised that medical applications are likely too far reaching for an iGEM project.[83] Other branches appear to have been influenced by the crash course, including those in the "uses of bacteria" grouping in which Tobey wrote "sense", "breakdown", "secrete", "memory" and "movement", each in its own strand that is also further branched out (recalling an emphasis on microbial metabolism). Other thoughts appear to have been inspired by practical sessions, including the "repressilator" and "predator / prey" systems off the "modelling" branch; the "black and white bacterial biofilm" off the "uses of bacteria" grouping; and the "taking + displaying pictures" arm. Reflecting Tobey's engineering perspective, the groupings in "modelling / computer logic", for instance, are far more

[83] Occasionally, this was said of synthetic biology in general. Multiple discussions with Cambridge advisors revealed their feeling that the field was at a very early stage and better directed towards applications in synthetic chemical production, environmental areas (biosensors, biodegradation, agriculture, etc.), art and design as opposed to medical applications. They claimed that the field was still too immature to reliably make products for direct human consumption. One exception, however, is the overwhelming support for the Keasling laboratory's anti-malarial application.

developed than arms such as "art" or "medicine"; Tobey was also considering ideas such as "EPROM"[84], "Turing machine" and "computer interface". Notably, Tobey had been influenced by the Dragon's Den session on biotech business as he considered "branding it well" to be an important part of crafting a good project.

Moving to the right half of this map, one can see some of the "existing BioBricks" that were considered as potentially useful in building a new biological machine, as well as some of the existing systems that have been built in previous iGEM years. Drawing attention to specific branches, Tobey considered that the available DNA library of parts offered up different types of "chassis" (yeast and *E. coli*); "odour production" (e.g. banana and wintergreen smell generators); "cellulose producing bacteria"; biological "battery" functions; movement functions (referring to the branches "magnetotaxis", "galvanotaxis" and "geotaxis"); "biosensors"; and the "taking + displaying pictures" system. I learned from the advisors that as the competition continues, ideas increasingly get recycled – projects on battery systems, electronics or biosensors consistently feature at the Jamboree. Unsurprisingly, the electronics-leaning ideas tend to appeal to physics and engineering iGEMers – far more familiar territory than diving into the daunting complexities of the real biological world. Without detailing this mind map further, what I find most important is that it illustrates – in a rather nice constellation – the wide range of possible ingredients that might go into a good project idea. Furthermore, it reflects the great influence that pioneering teachers of synthetic biology have in shaping future ideas in this field and reveals some bias towards an engineering perspective that is faced with the task of building with biology.

[84] EPROM is a type of memory chip (http://en.wikipedia.org/wiki/EPROM).

Finally, it should be noted that in the first few days, this particular map became a reference point for the whole team to evaluate specific ideas against – this was a tool for individual and group thinking.

After an hour or two of brainstorming, the students and I went downstairs to the departmental tearoom and talked through the group's initial thoughts. On this, and countless other occasions, the ritual tea time was invaluable for the team's developing of ideas and troubleshooting challenges; I also learned a great deal about group dynamics, watching how different points of view would clash or come together. In this particular session, a number of interesting points were raised:

- Some students agreed that the idea should originate from a real-world application;
- Some students thought the idea should be simple, yet clever, with emphasis on good design and building a solid, well-characterised system;
- Another student emphasised that the project shouldn't be about solving a 'grand' problem; after all, in a short summer project, 'are we going to fix anything *really*?'
- A biologist asked an engineer whether he could model something 'cool'. He replied, 'engineers model – if you tell us anything about why and how something works, we'll be able to model it';
- Some thoughts-in-progress were shared:
    - 'What if we could make self-camouflaging bacteria? You could maybe have a red-light sensor that in turn makes the bacteria emit

or secrete red.' Another student interjected: 'that would mean you'd need a bacteria that could sense different frequencies of light; and where would you find a gene for that?'

- 'Is there something to do with light sensing, photographic bacteria or bacterial tie-dye worth pursuing?'
- 'Apparently there is a strain of helobacteria that are attracted to green and repulsed by blue light sources for some reason…'
- 'Maybe we could get bacteria to secrete cellulose for scaffolding or creating cartilage?'
- 'Could we use directed evolution to find an antibiotic that bacteria won't be resistant to somehow?'

- A biologist reminded everyone of complexities that make many of these ideas unfeasible:
  - 'Bacteria are unstable.'
  - 'We need to think about what bacteria do well: sense, breakdown compounds, secrete, change colour.'
  - 'No project idea is possible if we cannot find the 'gene for' the function that you want to engineer into the system – this is about *genetic* engineering!'
  - 'Using mammalian cells or genes is too complicated and unrealistic.'
  - 'Biochemical pathways have a horrible tendency to turn to equilibrium as opposed to pumping out something in excess.'

Only a couple hours into the project, tensions were apparent between those dreaming up big ideas and those with a more grounded sense of the difficulties in

working with biological material; the sobering voice usually came from a biologist. After tea and discussion, students moved back to their individual research stations and carried on brainstorming.

Turning to other diagrams that illustrate specific ideas, Figure 3.2 is about making a biological "counterfeit bill detector". The idea originated from a biology students' knowledge that counterfeit US Dollar bills are made of starch, while genuine bills are made of cellulose. It was thought that if one could engineer a system that had two types of bacteria in it – one that was programmed to constantly produce amylase (the enzyme that breaks down starch into glucose) and another that was programmed as a glucose-sensitive sensor that would turn on green fluorescent protein (GFP) production – then one could make a biological machine that would fluoresce green upon its interaction with a counterfeit bill. Without going into much technical detail, what one of the students did after thinking about this basic plan was to search scientific literature in order to find a gene that triggers the production of amylase. The student found that the desired enzyme (amylase) does not naturally exist in the intended chassis (*E. coli*); however, the student also found online the sequence for the amylase-producing gene that exists in *B. fragilis* (a gut bacteria). The student wondered whether it might be possible to get the gene from *B. fragilis* and put it into an *E. coli* system to achieve the desired constant production of amylase.[85] However, soon thereafter

[85] Generally, iGEM teams acquire genes from the following sources: (i) the Registry, (ii) their own institution or other academic laboratories willing to share DNA, (iii) DNA synthesis companies, through which genetic sequences can be ordered, tailored and delivered via post (e.g. DNA2.0: https://www.dna20.com/; and Blue Heron: http://www.blueheronbio.com/). This is a vast library of possible material as scientists have been decoding genomes for over 30 years; thousands of DNA sequences are online (e.g. in GenBank: http://www.ncbi.nlm.nih.gov/Genbank/), ready to 'copy and paste' into a synthesis company's order form.

the student constructed a “drawbacks” list and this seemingly simple plan no longer looked so straightforward (note bottom right, Figure 3.2).

Figure 3.2: Counterfeit bill detector system

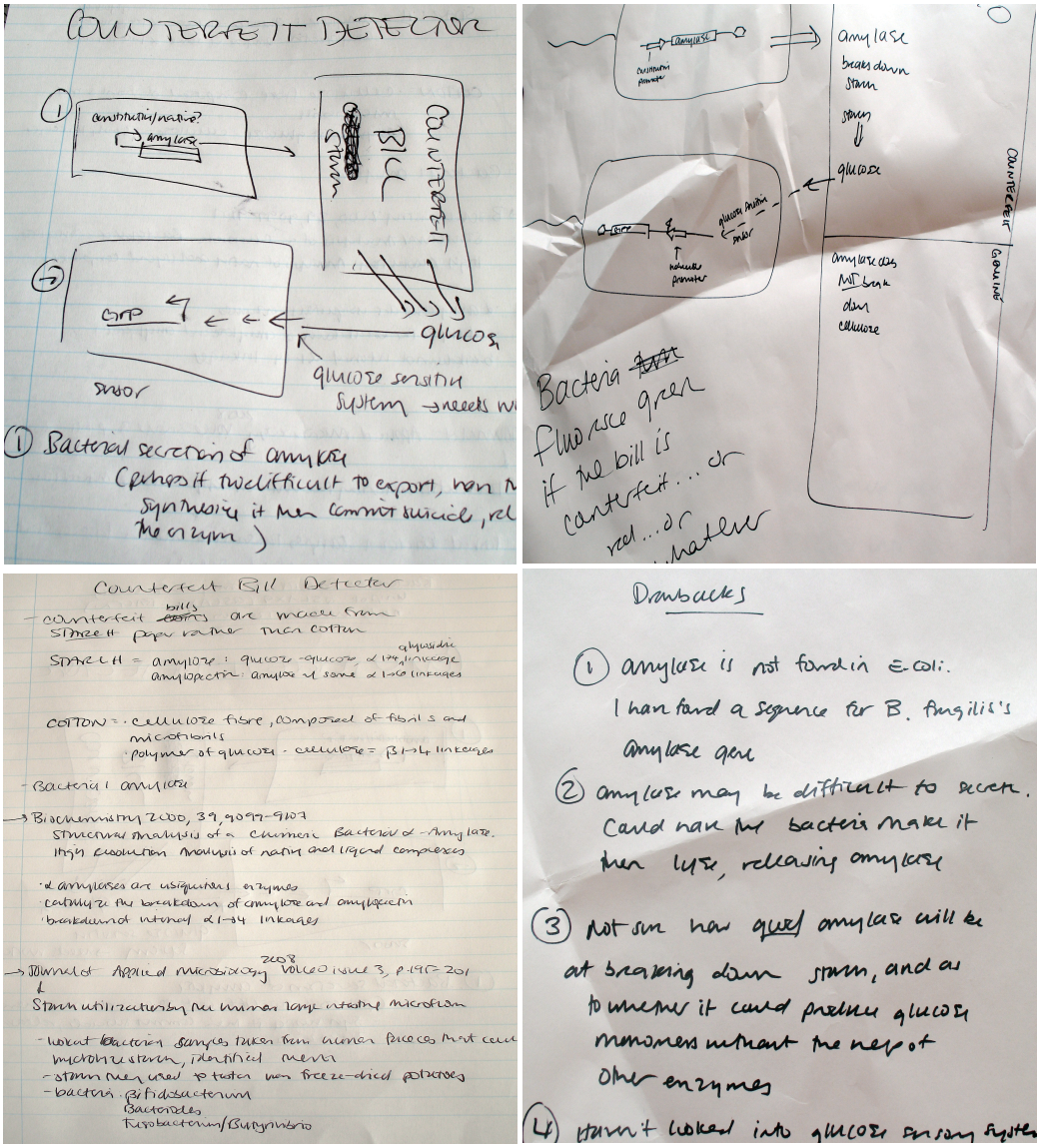
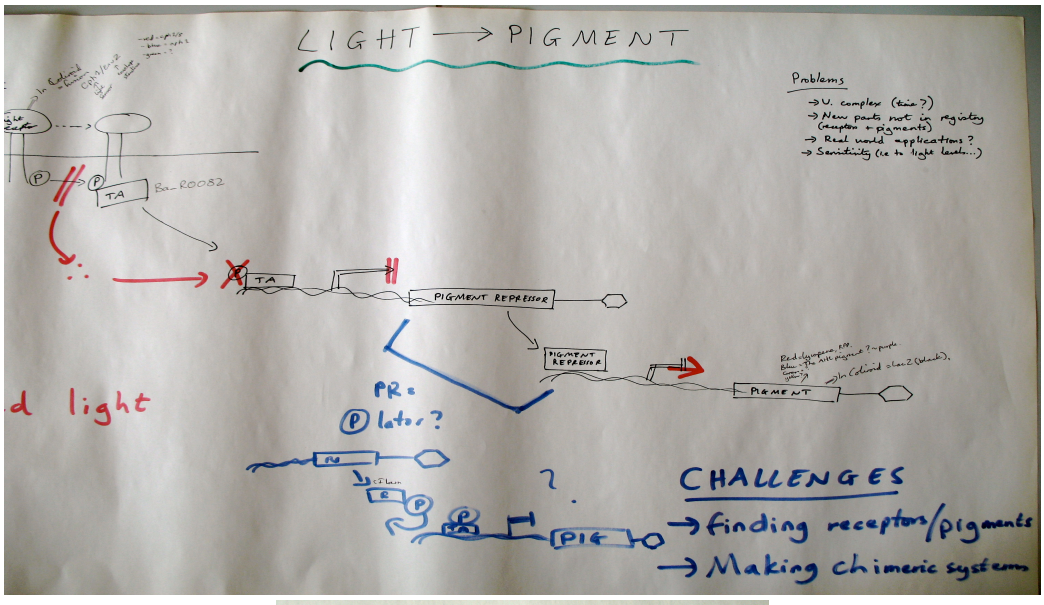
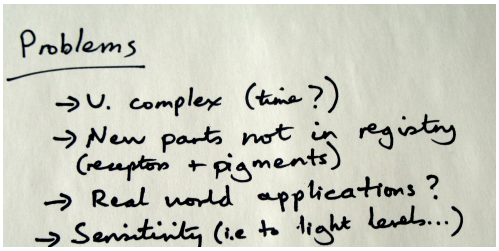


Figure 3.3 illustrates an idea for a light-sensitive sensor that would produce a pigment output to be used in a photographic system. Again, without the technicalities, the picture shows a hypothetical reaction relay, where the logic could go something like this: if you have a plate of bacteria with this envisioned light sensor - inverter - pigment system programmed into its genetic circuitry,

then when light shines onto the lawn of bacteria in a particular pattern, the light that is sensed will trigger an inverter logic gate and then the production of pigment in whatever pattern would be projected in the light. I should emphasise that the details are not what matter for the purpose of showing what dreaming up ideas for iGEM means. Again, I'd like to draw attention to the lists of "problems" and "challenges". When the students would later present the initial ideas to advisors, this potential project was rejected on the basis of being too complex and also too similar to work that was being pursued in another well-respected laboratory; however, the idea of pigment production was plucked out of this system and highlighted as both interesting and feasible to consider further.

Figure 3.3: Light to pigment system





Let me clarify a few points of analysis, before further illustrations and the team getting to their 'light bulb' moment. The drawing and writing out of thoughts on paper was, in my view, the most interesting tool for thinking used by the Cambridge team.[86] These diagrams illustrate a point of origin in ideas – they have materiality to them, a certain ontological status. Mind map ideas have had no inherent reality 'out there in the world'; yet, they start a process as they are drawn, connected, explained to peers and developed with the incorporation of feedback and new lines of research. Students used this exercise to bring together what they had learned in the course, while also breaking out to uncharted territory in playful and creative ways; they mapped in order to understand and organise their thoughts when the array of possible fields for brainstorming seemed endless. Mind mapping made certain things thinkable while allowing realisations that most ideas must terminate – too many "drawbacks", "problems", "challenges" (usually owing to biological complexity and time constraints). These figures also show how disciplinary leanings shaped certain individuals' thinking. Engineers often illustrated in streamlined, simple ways, using graphs and circuit diagrams where possible; biologists tended towards writing out ideas and using illustrations of bio-chemical pathways.

It has been a great challenge to select only enough photographs to illustrate what it means to creatively construct project ideas for this iGEM group as they had, over the course of only two intensive brainstorming days, generated over twenty ideas that had been researched and drawn out in some depth. Appendix IV has additional photos but, as a teaser, here are some titles of other ideas generated at

[86] Though I choose this focus, it was not this group's only tool for thinking. The team also worked on their Wiki, presented to each other, researched online, read and summarised papers and bounced ideas casually off each other and advisors.

this early stage: “obedient bacteria”; “incorporating a parasite into a predator-prey model”; “wave pulse bacteria”; a “bioclock”; a “glucose-to-cellulose slimming treatment”; “self-destructive plasmids”; a “heavy metal sequestration system”; a “land-mine detector”; a “project based on game theory”; a “3-D biological printer”. One can perhaps appreciate from such a list of dreamt up biological machines just how creative this early phase was, as students worked with a huge range of real-world or fun inspiration, combined with their knowledge base and research.

On the third day, after intensive brainstorming and only two short meetings with the supervisors – who, at that point, provided encouragement, suggestions of references and subtle steering towards more realistic projects – the team produced a list of contending projects. It was then time for the advisors to step in, act as gatekeepers and tell the team which ideas were feasible or not. Commenting on the advisory role at this stage, Frederick said:

> It is important to give the students some space at first. Then, in actual fact, it’s important for the faculty – once the students have had a brainstorm – to provide a bit of pruning and reality checking.

Although each short-listed idea was pitched to the advisors, the resounding message of the meeting – taken on board by all students, except one, who wanted to go for a rather lofty and ambitious project – was that choosing an idea came down to feasibility. The advisors were the ones with expertise and experience in making such a judgement. Senni told me:

> In the first week of brainstorming, we realised that what we lacked was not the ideas… but, the thing is, how exactly feasible are those ideas? At that time, most of us did not have lab experience and we did

> not realise how difficult it is to come up with a working system. So, after that, two advisors mentioned that one of the common themes in the systems we were brainstorming was colour. So, we zoomed in on colours. It was do-able so we did a colours project.

Tobey also commented on feasibility:

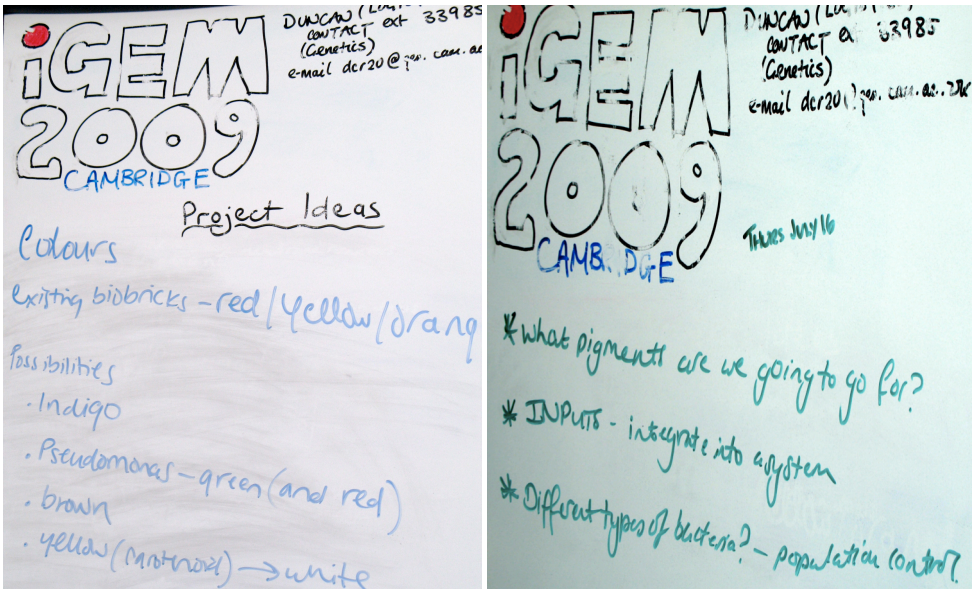
> At the beginning, without the knowledge of the biologists we would have gotten nowhere because you need someone to say what won't work… The engineers and physicists could think up ideas but it was really down to the biologists to say whether it was feasible or not.

The decision to pursue a project based around pigment generation made sense for a number of reasons: the faculty thought the concept was biologically feasible (in theory) and there were already bacteria with pigment genes in Douglas' laboratory that students could use. There was something playful about making colourful bacteria, which would appeal to an iGEM audience and there are a number of useful applications that pigment production could potentially link to (an output for biosensors being one). The Cambridge team had arrived at their 'sticking point'.

Figure 3.4 shows the white board only three and four days into the team's work. By this point, the group had a list of possible colours to research further and they started to think about what kind of larger system a pigment generator might be built into. For some, it was a great relief to be started on a more specific path (though, as Chapter 4 shows, there was still plenty of evolution in the project):

> At the beginning, I wasn't good at thinking up the ideas for the project. *I was good when I had something to do and then I went ahead and did it.* – Eleonore

Figure 3.4: Colour pigments stick

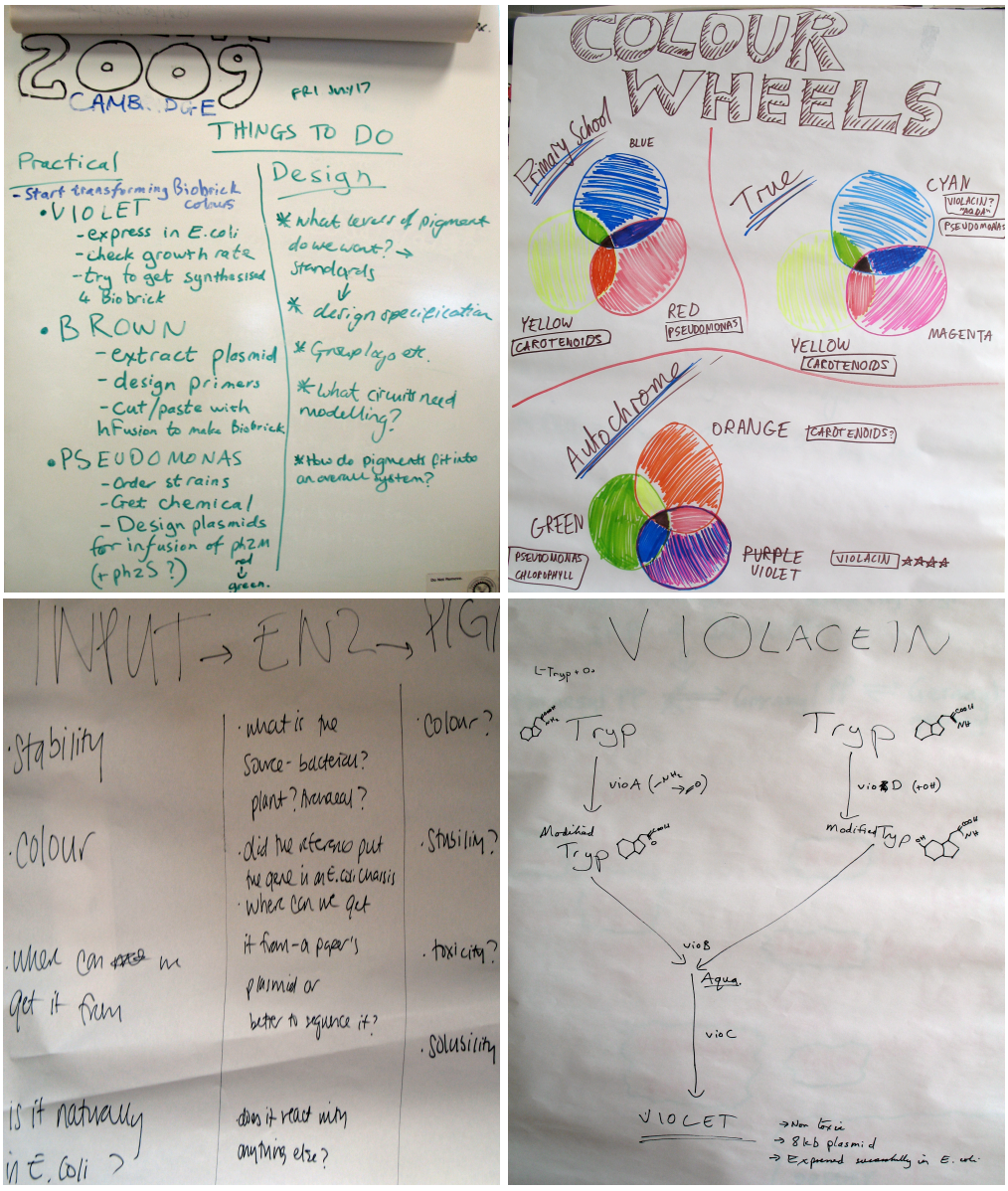


Before discussing the Imperial College team's dreaming up ideas, a few more illustrations from the Cambridge team foreshadow things to come, as ideas continued to evolve and the group set up experimental processes. By the end of week one, the group was coordinating regular To Do lists, delegating tasks among team members. The students decided to start working on making at least two pigments – violet and brown – and they looked into acquiring strains of pseudomonas bacteria that might allow them to build a red-to-green colour system. Students continued to think creatively and in illustrations. For instance, they hypothesized about how the mixing of different primary and autochrome spectrums might help them construct different combinations of three colour producing systems to generate a variety of pigments (Figure 3.5 top right).[87] The bottom left of Figure 3.5 shows how students defined three components in their imagined system – input, enzyme and colour – and developed a list of questions to tackle about each of these parts. The final picture in the figure below illustrates an

[87] It was suggested that perhaps the group could try expressing colour combinations in the same cell or they could try mixing three different cell types on the same Petri dish.

enzyme pathway for violet production, used by one of the team's biologists to start designing experiments. List-making and drawing diagrams to develop conceptual ideas as well as laboratory protocols remained a key feature in the thought processes of this team as their project progressed; several other practices, processes and 'tools for thinking' evolved later.

Figure 3.5: Beginning to evolve ideas on colours



3.2 Dreaming up ideas at Imperial College

Introducing synthetic biology in iGEM try outs

2009 was the second year a full undergraduate course in synthetic biology was offered at Imperial College; unlike at Cambridge, however, taking the course was not a requirement for all iGEM participants (only half of the final team had been in this class). Having already discussed key concepts in synthetic biology in the section on Cambridge's crash course, I address another kind of teaching and learning that occurred during the Imperial College iGEM try outs.

Recruiting for the team began in February (well before the official start in July), with advisors endorsing the excitement of iGEM and synthetic biology to a group of over 50 top science and engineering undergraduates. After that initial pitch, students returned for a series of four try out meetings in gradually smaller numbers (a self-selectioning occurred, with many deciding for themselves that they were not right for the team). These meetings took on a similar pattern: students worked in small groups, brainstorming for about an hour (as advisors circulated the room, listening in, asking questions and giving advice), before they presented and faced critique from superiors and peers. Dozens of interesting, some far-fetched, ideas surfaced. Along with the imagining of blue sky synthetic biology possibilities, ideas came under scrutiny and were moulded by the advisors' comments. Eager candidates flexed their creativity, group work and presentation skills in ways that most of them never had; these meetings, therefore, also provided advisors a basis from which to select the final team of eight (from about 15 who remained by the time selection occurred).

Before describing some dreamed up ideas that arose during try outs and showing how the possibilities of thoughts were shaped, I shall first note the kinds of intellectual technologies that were most pronounced in this group. Though students occasionally drew out mind maps, they did not do so on nearly the same scale as the Cambridge team. Discussion in small groups, presenting and using online forums were far more important tools for thinking among Imperial College students. The first forum (using Google Documents) was set up after the second meeting (mid-February). Online, candidates shared research, organised and coordinated meetings, posted recommended readings and websites, taught each other, made comments on and expanded ideas. The extensive online presence (with forums often populated by keen students working in the middle of the night, on top of their normal study routines) meant that the group could get right down to business at try out meetings.

Turning to an idea that began at that second meeting – and one that gets partly translated into the final team's project – the iGEM candidates imagined a system of "Bacteria for Long Term Drug Release". Online, students contributed to a proposal that envisioned a symbiotic relationship between human beings and drug releasing bacteria and that would cure ailments. Realising that consumers might dislike the idea of ever-proliferating bacteria inside them, the students thought about how to engineer a "programmable time of living" for these microbiological machines in which they would "release a certain chemical to tackle a certain disease". The goal then, as the team initially conceived, would be to make bacteria that survive in humans only to complete their curative job (saving people from the inconvenience of taking a pill or undergoing cumbersome or ineffective

treatments), to then die, be digested and exit the body via defecation. The team claimed that this project vision was so appealing in terms of its modularity and extensive application interchangeability – perhaps their bacteria could eventually be used to produce *any* compound to cure *any* disease. There were, of course, challenges: (i) how does one create a programmable lifetime for bacteria; and (ii) how does one find bacteria that can withstand the low pH of the human gut? Only a couple of meetings in, the aspiring iGEMers had clearly recognised that grand project pitches, an engineering approach and an addressing of possible challenges were all crucial to receiving positive feedback from advisors on their ideation process.

As meetings continued from February through May, students developed a huge number of ideas – far too many to describe here, from complete non-sense to the fun and frivolous, to the impossible to complete, to 'save the world' scenarios. Highlights are provided in Figure 3.6.

Figure 3.6: Further examples of dreamed up ideas from iGEM try outs

Project idea / title	Basic description
Bio-radio	Using bio-electricity (produced in mice and fish), the idea was to create a biological radio that somehow used wireless communication and cell communication. A student claimed during a pitch, 'if neurons can send and receive wireless signals, we might be able to monitor biological systems wirelessly, even communicate with each other without speaking'.
Living battery	A student proposed to design a 'self-recharge or regeneration mechanism'.
Borane-based fuels	With the knowledge that a 'potential and promising hydrogen store is in ammonia borane, which can release hydrogen with the aid of Nickel and Ruthenium based catalysts', a student wondered if a biological machine could be created to create fuels by co-opting this pathway somehow.
Biological oscillator	Build an oscillator device that could be used in timed drug release.

Bioimaging	Make a biological machine that uses bioluminescence to serve as a display / imaging system. This kind of machine might be used either in diagnostics or in a novelty / commercial scenario (e.g. bio-digital-photo frames, holograms, 'psychedelic mice' aka 'animal display systems').
Biofuels + waste management	A system to make biofuels but not just tackling the energy problem, the proposal included addressing the question of waste management. In a nutshell, the goal was to find a pathway that could be used to convert rubbish into hydrocarbon fuels.
Biofuels + self-directed evolution	The aim of this project would be to improve the production of cellulosic ethanol in the following way: (i) identify one or more genes to improve the production of ethanol and (ii) construct a system to improve (i) over time (aka directed evolution).
Bactoshave	The idea here involves engineering a skin bacterium to degrade hair and possibly to generate sunless tanning molecules.

With these sorts of examples in mind, what is perhaps more interesting to consider is the influence that critiques of pitches had in teaching students what ingredients were needed for good project ideas. Repeatedly, the advice from top-tier authorities[88] – Roger, Bernard and John – was that a good iGEM project had to keep in mind the following essentials:

- New ground must be found and broken – 'judges won't want to see the same old biosensor';
- There needs to be wow factor – incremental steps are simply not enough to do well at the Jamboree;
- The project ideas must be grounded in proteins, genes and DNA that is possible for you to get hold of and work with;
- The project must be about *engineering* – there's got to be data and results.

[88] The hierarchical ranking amongst advisors became evident – Bernard and Roger at the top, John right below, and Olivia, Max and Pierre below. Olivia, Max and Pierre spent time with iGEMers daily; meetings with 'the Profs' were more occasional (usually weekly) and took a serious tone.

Noting a few specific criticisms of ideas in the chart, advisors reminded students that an idea like ‘bactoshave’ was completely ridiculous – why, when there are cheap and good products for shaving and tanning readily available, would anyone seek to develop a synthetic biology application to replace what already exists? Similarly, the bio-radio idea was rejected outright – it was completely implausible and people in the room barely contained their laughter as one student tried to make the suggestion that remote communication between humans might be possible by taking advantage of bio-electricity properties in a rare fish species. Certain biases of advisors also came through during the try outs – hints were often dropped that ideas around medical or biofuel applications might be particularly suiting to Imperial College’s industrial-driven ethos. Comments from superiors – sometimes in the form of subtle steering, other times in the form of strong criticism or emphatic statements about the radical potential of engineering biology – shaped the ways in which students further mapped out potential projects.

By the time students experienced a couple rounds of brainstorming, presenting and critique, the online forum showed features in thought organisation that ran through most entries: there would be a short pitch (usually problem - solution), background information, some ideas on methodology and challenges, a summary or mission statement, applications listed, tables, diagrams (e.g. of chemical or bio-molecular pathways) and points of contact. Students also became conscious of presenting their ideas through the engineering cycle (as advised by Bernard) and demonstrating principles of modularity and abstraction. Thoughts became more organised, tried to tick essential boxes and were pitched in an increasingly

competitive fashion as try outs proceeded. Students wanted to sell their ideas and themselves as worthy candidates for the final team cut.

Before moving to explore the official team's starting days, where they continued and enhanced this dreaming up of ideas, it was clear that certain roles began to take shape during this initial phase; this was evident not only in-person, but also on the forum. For instance, the following posting clearly illustrates how one student, Zach, made early efforts to stake a leadership position:

> Firstly, thanks for your emails; it's good to hear that so many of you are up for making this work. The first tranche of research has been divided up as follows: [sign-up list]… As you identify genes of interest, please add your info to the gene table below. [Extensive tables and diagrams follow.] … Moving forward: At the end of last year, I wrote a dissertation on the prospects of cellulosic ethanol so I would be more than happy to run a crash course on the subject… If you are interested in meeting up to discuss an iGEM project relating to biofuels, just sign your name and I'll email everyone to work out a suitable time.

Character traits were taken into consideration in the selection process. Advisors told me that it was very important to have a team with the right balance, not only of disciplinary expertise, but also of personality. They needed some leadership, but not so much that strong characters would collide too often, and they wanted that balanced with students who just tended to get to work.

The advisors too began to reveal their biases and personalities during try outs. Roger and John had words of wisdom on biology, as did Max and Olivia. These teachers continually reminded students of biological complexities that would make most of the proposed ideas impossible in experiment. Bernard and Pierre, on the other hand, held a strict engineering view. They wanted to know about data, results and applications that an idea might lead to. Bernard and Roger – two

eminent Professors – emphasised repeatedly that '*This is a competition and, here at Imperial, we are a pretty competitive bunch!*'

In the early brainstorming sessions, I have described how a competitive spirit and clear ambition to solve rather grand-scale problems is at the heart of the Imperial College iGEM team tradition. Certain thought patterns were taught and taken up by students over the course of recycling through brainstorming work, presentations and critiques. The Imperial College way to think about and present synthetic biology was to emphasize a systematic, rigorous and competitive approach. Online discussion forums were a key intellectual technology utilised by the group; indeed, this continued to be the case for the official team. Finally, I've indicated how some roles began to take shape, even in the first few meetings.

From blank slate to an idea that sticks

After about three months of try outs, the final team of eight were selected; they continued to meet periodically to brainstorm, even during their exams (an early sign of deep commitment). But, let's skip forward to the start of the official iGEM project time. On day one, the first order of business was for students and advisors to have a quick briefing at 'base camp' (Figure 3.7) – the desks got positioned into a team circle and the meeting began with introductory remarks from advisors. Roger started out saying 'Congratulations – you've made it', quickly followed by the counsel that 'this will be an intense time'. The first couple weeks of iGEM are typically very hard as 'nailing down a project is challenging, frustrating and time-consuming'. He continued:

> You must have faith in the process – one that is tremendously interesting and creative… At Imperial, we have a tradition of starting

> from scratch – today, you've got a blank page. The goal here is that from a blank page, you make something novel, new and exciting that actually works in the lab. We eventually need something that delivers results and has data… *It is a competition!*

Other advisors who described iGEM's uniqueness in its high level of free-thinking echoed similar comments of motivation and guidance; it was also emphasised that competitive projects had deliverables ("hard experimental data") and "sparkle". Finally, one advisor counselled, "You must be prepared to deal with critique from leaders, as well as failure – your ideas may simply not turn into reality".

Figure 3.7: Imperial College team's 'base camp'

After the somewhat emotive speeches, students tightened up the circle, advisors left and the group proceeded with timetabling and research. The team oriented themselves around suggestions in a two-page document, given by advisors,

entitled ‘Getting Started’. Recommendations included setting up a journal club, conducting student-led presentations and tutorials and investigating old iGEM Wiki’s, The Registry and synthetic biology literature. The group delegated who would look into specific areas, lead journal club discussions and also decided to use social media to track their project (Twitter and YouTube accounts ensued). Then, it was off to the computer room – this familiar scene is illustrated in Figure 3.8. It was a solid two weeks that students spent much of their time in front of computer screens as they researched, communicated and imagined ideas for their biological machine.

Figure 3.8: Researching in computer room

As the dreaming up phase continued, the group focused on developing their online forum[89] and presenting to each other. In brainstorming, the four engineers or

[89] At that early point and up until late in their project, students worked on http://openwetware.org/wiki/IGEM:IMPERIAL/2009. The team could have used their official iGEM Wiki site early on but were warned by Bernard that, to protect their ideas from being copied, the lesser-visited OpenWetWare site should be used to start.

computer scientists often paired up with the four biologists of the group. Through this, students gained an appreciation for the partiality of any given individual's perspective and understood that they would need each other's different expertise in order to build a project that satisfied the requirements as they had been laid out. Having not all taken a synthetic biology course, the team also formalised peer-led tutorials in order to bring everyone up to speed on crucial basics: an introduction to synthetic biology (a 30-minute whirl-wind overview, given by a student who had taken the formal course); a lesson on the Central Dogma; a tutorial on laboratory techniques; and a workshop on computer modelling. Notable synthetic biology papers were also evaluated in journal club sessions during the first two weeks. For instance, the work on engineering yeast that produce the anti-malarial compound artemisinin (Ro *et al.* 2006) was held up as a favourite example.

Thoughts for a project proposal continued to develop from selected good ideas (validated by advisors) that came up in try outs, as well as broke into new directions. The team tirelessly researched useful genes, enzymes and missing links around ideas such as hydrogen-production from bio-mass, auto-encapsulating pills, making a 'bacto-camera', 'bacterial sun cream', biological batteries and many more. Students developed criteria lists and ways of scoring ideas so that when pairs came to present to the rest of the group, there was a systematic routine for feedback. Students voted on scores (0 being useless, 5 being average and 10 being excellent) for each other's project pitches that were evaluated for originality, feasibility, usefulness, "showing the union of engineering and biology" and market appeal. In my observation, the systematisation, organisation and scrutiny to which students subjected their work were remarkable. Between

lessons, online research, journal clubs, brainstorming sessions and presentations, the team was working long days and yet students still arrived every morning with more work that they had done on their own in the evenings. I was thoroughly impressed by the effort to find that sparkling project.

However, the team had great difficulty in getting to the sticking point idea, in no small part owing to high standards set by advisors. Leading up to the project idea's finalisation, there were several meetings in which students faced critique and re-evaluation of their progress – the interrogation from Max and Pierre was daily and, at least every couple of days, their ideas were evaluated by Bernard, Roger or John (sometimes all three), for the real authoritative opinions. In the face of a great deal of time and effort in dreaming up ideas, upon presenting to their superiors in the first two weeks, students were continually reminded of ingredients that any particular idea failed to factor in to a satisfactory level (a redundant-sounding list):

- Where's the application? What is the big thinking?
- That is too trivial – what you want is a 'save the world' idea!
- There needs to be more emphasis on the engineering cycle.
- What are the desired genes and proteins you'd use in experiment? Can you get hold of them?
- Have you accounted for the biological complexity involved (e.g. referring to host-chassis relationships or the diverse, unpredictable and noisy natures of bacterial systems)?

The bottom line for an ideal iGEM project in light of the Imperial College competitive spirit was that it must be both grandiose in it's pitch (something that

could, in theory, solve pressing global problems) but also have some doable experiments that would give the team data and results to bring to the Jamboree. These two factors are particularly at odds when, upon taking the next step to turn an idea into designing experiments, a seemingly endless set of biological complexities comes into the picture.

Despite what was an uphill battle at times – as the mood often swung from incredible excitement at light bulb moments to real depression following some harsh critiques – after two weeks of solid work, the iGEMers arrived at their project's core concept. They would engineer an auto-encapsulation property into bacteria that produce a compound, *X*, in order to solve a problem, *Y*, in the gut. This idea was based on two interesting engineerable functions (self-coating and drug-producing bacteria); it could be pitched as a generic drug production platform (in theory), showing a good manufacturing potential; it was modular, making it amenable to an engineering approach. By week three, there were occasional approving comments from senior advisors: the team was told, 'you've got the bare bones of a good project here'. However, there was a great deal more work to do and pressure remained high. By the next meeting, students were instructed to show that they had "really drilled down into the different modules" – advisors gave the students two days to get full specifications for each module, "knowing everything about the genes and enzymes [they] would want to use". Furthermore, the team was expected to have outlines of proposed experiments and, perhaps most importantly, an application "with a compelling and emotional

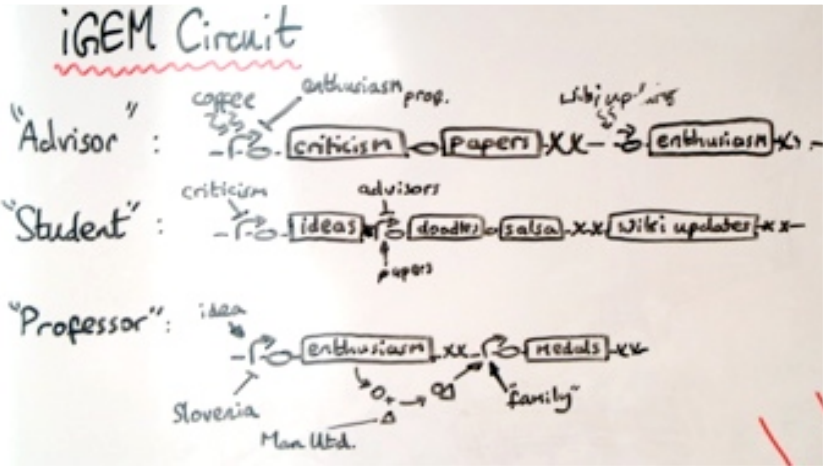
message" nailed to the project.[90] The project continued to evolve and overlap with experimental stages and so the reader will find the ideas development theme continuing into Chapter 4. There is one other important point of discussion about this early stage.

I'd like to draw attention to some social dynamics and character traits that were revealed during this intense beginning. Starting with the iGEMers, all of whom proved to be incredibly well accomplished and ambitious – many were on prestigious scholarships; all had some ideas about where they'd like to pursue graduate studies. Andrew and Zach took turns being the head evangelists of synthetic biology and leaders of the team, both having described their dreams to venture into biotech start-up companies. The first few days resonated with optimism – for instance, as Zach joked that the team "should be preparing the acceptance speech for the Jamboree" – but students still worked hard. Then, when more difficult times set in after the occasional disappointing meeting, students tried to pick up each other's spirits. A sense of comradery was built over casual lunches on the Imperial College quad lawn and in the occasional evening of team salsa dancing. In field-notes, I noted also being quite impressed that even two or three quieter students found their voices quite quickly and were recognised as having an important role. The team knew that they needed each other's perspectives in the work and, at least at the beginning, the group got on as new friends.

[90] The emphasis on having a sentimental message was over-the-top, particularly as advised by Bernard. He once said, "working on solving AIDS in Africa or curing cancer – this is the stuff that wins!" Some students were suspect of such comments but overall, the team felt obliged to play into the Professor's advice.

Of the advisors, Pierre quickly became know for his tough love feedback, displaying impatience as he sat at the back of the room, arms crossed, leaning back in his chair, one foot perched on the other knee, often fiddling with a pen. As he worked largely on the computer too, Pierre had the role of primary oversight in the first couple weeks and gave a great deal of help to the students. Max emphasised biological complexity; however, as a previous iGEMer, his suggestions usually rang with positivity and empathy and were much appreciated by the team. Olivia took a more neutral stance – constructively critical in her feedback and without attitude. As an expert in the laboratory, Olivia repeated one major point to the student: "keep it simple!" In the team's oscillations between optimistic dispositions, busy flurries of research and difficult periods of rejecting and re-evaluating ideas, one student doodled the 'iGEM Circuit' cartoon (Figure 3.9).

Figure 3.9: 'iGEM circuit'



This cartoon plays on the style of synthetic biology genetic circuitry. Highlighting the "Student" circuit, it reads "ideas" get started (or inhibited by "criticism"), which get fed into by "papers" (or inhibited by "advisors"), which turns on "doodles", leading to the production of "salsa" (referring to how some students go salsa dancing together to let out their iGEM frustrations). The "Wiki updates" segment stands alone, as a separate functional unit, with stop codons on either end.

Conclusion

Conceptually, this chapter has been oriented around two borrowed notions: Bachelard's (1984) phenomenotechnique and Miller and Rose's (1990) intellectual technologies. To participate at iGEM, ideas for constructing new sorts of genetically engineered machines must first be conjured up in the mind before they are turned into real experimental processes – and this is done with technology and application in mind. I have described what is more an exercise in *creative thought* than in hypothesizing, deducing, or practicing on already existent biological phenomena. iGEM students are challenged to find their materials from a vast pool of genetic functions and think about how to put them together in novel, functional and exciting ways. This activity of dreaming up ideas is not abstract – there is materiality and ontological status to the envisioned projects. I've illustrated how ideas originated and were developed using tools for thinking: drawing mind maps, making lists, sketching pictures, using online forums and conducting presentations. These various media gave imaginative thoughts points of attachment, so they could be understood, extended and re-evaluated in multi-disciplinary teams that also had advisory oversight (in differing degrees at Cambridge and Imperial College).

An important condition on the possibilities for dreaming up iGEM ideas was how students were taught to think about synthetic biology and the competition. At Cambridge, the crash course was crafted in an attempt to evenly equip students with introductory knowledge, but even more, to inspire and excite. The involvement of designers and myself in the course, along with diverse practical sessions and some rather unconventional lectures all sparked the Cambridge

team's initial creative brainstorming stage. That team's week one output saw them arrive at an idea for a colour generator and ready to start laboratory work.

With the Imperial College group, try outs shaped a particular way of coming up with potential projects. Students were taught that their pitches ought to demonstrate rather grand scale, problem-solution thinking, yet still with competitive deliverables. Coming up with a project – under high standards set by advisors, without the entire team having a thorough grasp on synthetic biology – was challenging. Overcoming their first wave of major difficulty, this team arrived at their sticking point idea, to engineer a self-encapsulating drug production system, in week three.

Understanding how these groups were taught and how they developed project ideas was embedded in human characteristics, institutional cultures and social dynamics (further elucidated in the coming chapters). I have introduced how different ways of approaching the project at hand were especially apparent in comparing engineering to life science views. Another interesting point of comparison was in students' self-identification as 'creatives' (who enjoyed dreaming up ideas) or more so 'doers' (who were eager to execute a plan of action); this was particularly evident at Cambridge. Students began to get to know each other too – they discovered each other's strengths and weaknesses and found how different skills and knowledge bases could compliment or collide. Many were challenged by the amount of free rein thinking that is given to iGEMers, something rarely found in conventional undergraduate engineering and science courses. The diversity of talents and perspectives enhanced the imaginative nature

of ideas that arose. There also had to be a certain taming of imaginations in this process. Leadership within teams was needed, as were habituated ways to organise thoughts and tasks; advisors also provided reality checking of ideas for feasibility, and sometimes very direct steering.

Leading into the next two chapters, Hacking's (1983) position as a realist about entities and an anti-realist about theories is noteworthy. The brainstorming and arrival at ideas that has thus far been illustrated is theoretical. Though I have argued that thoughts can, in some ways, be materialised in mind maps, online postings, presentations, etc., at the dreaming up stage, they still do not amount to real existing, causally powerful entities. No strategically engineered, pigment producing bacteria existed, nor did a self-encapsulating drug production system – even though teams developed theories about how such biological machines might work and with what components. In the next chapter, I shift from the theoretical into experimental realms; then, in Chapter 5, the reader finds that some real entities are made. In that domain, another kind of reflection about new living synthetic biological forms is possible.

4. EVOLVING IDEAS INTO DESIGN AND EXPERIMENT

This chapter enters the territory of purposeful design, experiment and computer modelling; the iGEM groups' evolution of ideas, team dynamics, individuals' skills development and laboratory practices are examined. Interestingly, a conflicting understanding of biology as both discretely engineerable as well as impenetrably complex emerges. This stage of practice also reveals divergent views about how to understand and perform synthetic biology across the two institutions.

4.1 Evolving ideas at Cambridge

The project develops

> Right now we're just looking at output; this isn't yet a full *machine* and this *is* the genetically engineered *machine* competition!
> – Chelsea

Following the idea to make bacteria produce pigments, the team knew they would have to start experimental work, while enlarging their project vision, attaching it to an application – even if it were only hypothetical (as most iGEM work turns out). The evolution toward ever-more practical ideas also targeted the competition's general ethos. The process started with a suggestion to "paint a bacterial wall"; this was followed by a proposal for a "bacterial colour printer"; another student reminded everyone that the aim was to do something that 'takes inputs 1, 2 and 3 and hooks it up to outputs x, y, z, making a machine that is modular and interchangeable so that you can have several possibilities and other people can build on the work'. Finally, despite a brief flurry of anxiety, the group had their first project overview on their Wiki by the end of week two:

> Previous iGEM teams have focused on genetically engineering bacteria to respond to novel inputs – for example light, or biologically significant compounds. There is an unmistakable need, therefore, to also develop clear, user-friendly outputs, especially for use in biosensors. The most popular output is the expression of a fluorescent protein, detectable using fluorescence microscopy. However, how much easier would it be if we could simply *see* the output with our own eyes? The Cambridge 2009 iGEM team is engineering *E. coli* to produce a range of pigments in order to equip future projects with better, more reliable, discrete outputs under logic control. Further, our bacteria utilize a shutter mechanism that guarantees pigment production after just a brief exposure to the desired input.[91]

This was an idealized project idea that continued to change. Shortly after this Wiki posting, one student remained dissatisfied with the extent to which the project looked exciting and innovative: "Isn't it too basic? We've got engineers here – shouldn't we be able to get a more complex pathway, with more than one arrow?" The desire to 'go bigger and better' led to a number of days when a few team members worked tirelessly with add-on proposals. Although the advisors all believed this extra work was unnecessary and 'de-railing' the team, they did not stop the students from making their own mistakes.

> It seemed like every day they were considering something new for a while and not necessarily for any reason… a step back. But, at the same time, these set-backs are part of the iGEM process – students consider a bunch more information, read a whole bunch of papers and they have to carefully weigh the excitement and feasibility balance of their project. – Andy

After researching the addition of a "shutter mechanism", various switches (a toggle-switch, a bi-stable switch, a latch), a kind of "engineered memory" and a "population control device", all these potential add-ons were rejected as being too complex, especially given the limited project time and capacity of the team. However, one add-on would make the group's pigment-producing *E. coli* just

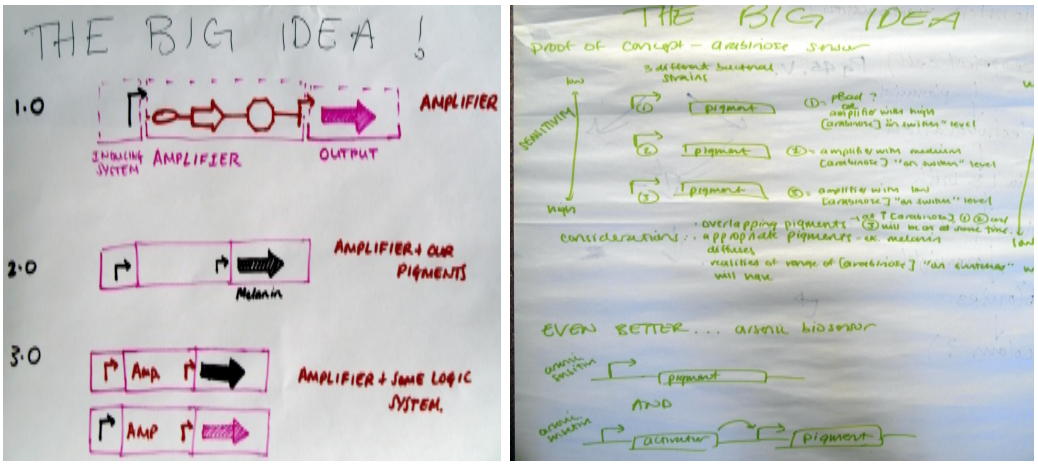
[91] http://2009.igem.org/Team:Cambridge. Note that this quote is from an early posting on 22 July 2009. It was later edited and so only the final version appears on this site.

that extra bit more sophisticated, and it was feasible: the students decided they would resurrect the Cambridge 2007 iGEM project and work on improving that team's amplifier system. The basic idea was to develop the previous work and customize it as a 'sensitivity tuner' that would slot into the overall project design: [sensor] – [sensitivity tuner] – [colour], as [input] – [processor] – [output]. Students suggested potential mechanics for this tuner; their initial vision was that it could be functionally programmed to detect meaningful concentrations of a given input. The overall project – in its goals and deliverables – is discussed in the next chapter; for now, it suffices to understand that the project conception by the fourth week was a pigment production system that would have a set of tuning devices, making the students' work especially relevant to biosensor applications.[92]

While the team settled on their "big idea" (Figure 4.1), at least three students already had biological laboratory experiments underway. Early entry into both 'dry' and 'wet' laboratory practices and processes (discussed in an upcoming section) meant that the team's project evolved in parallel with successes and failures in experiments. A final important point about the idea evolution is that the team continued to draw mind maps, use the white-board, make lists and generally plaster their workspace with reminder notes.

[92] http://2009.igem.org/Team:Cambridge/Project.

Figure 4.1: The Big Idea



The team evolves

As ideas developed over the summer months, so too did group dynamics and individuals' skills. One of the most significant team challenges was in learning to work productively between various disciplinary views – dealing with technical "language barriers". Figure 4.2's interview excerpts (taken from the project's mid-point) illustrates differences in disciplinary perspectives:

Figure 4.2: Comments reflecting disciplinary perspectives

Students of biology	Students of engineering
"[The challenge] has mainly been the vocabulary. They all have words for how devices work and synthetic biology is all about how to put devices together. So, suddenly, you are throwing words around like 'adaptor'… It is funny because, in the lab, I'll be pipetting and doing my thing really quickly and Alex is really only just learning how to do that. Then, Alex will start drawing electrical diagrams – bang, bang, bang... and I'll just be sitting there, struggling to understand."	"The biggest challenge was probably the learning curve at the start – for me. All these big biology words that you just have to learn!"
"Making everyone with a different background understand the project – that is something that we're still struggling with, but that was also what was so interesting… Alex will look at the data and, where I'm interested in only if it works, he is interested in the slope and the thresholds. The different	"Not one person knows everything that's going on – we all work in our own little areas more. So I found myself not needing to learn some of the biology and then others don't need to learn MatLab [a computer modelling program]."

perspectives really enriched the project but it was also very challenging to get everyone onto the same page..."	
"Biologists are very insular – we like to play with the bacteria and get our results and that is it. But, those guys [the engineers and the physicist] know how to program and they have new ideas. You were there when Tobey set up the idea for the whole new software programming thing. I don't think a biologist would ever devote the time or even know how to begin doing that kind of thing. It is just great that people with other areas of expertise are getting involved with biology and improving it in ways that biologists themselves would never be able to do."	"It took me a long time to explain to some of the biologists what I was doing and still sometimes, no matter how well a biologist explains what they're doing, I sometimes don't get it. Sometimes I just decide not to bother. Otherwise, everyone has a vague idea and that is all that matters… At the beginning, without the knowledge of the biologists we would have gotten nowhere because you need someone to say what won't work for whatever reason."
"Programming is my ultimate weakness – I really can't wrap my head around it… It's really interesting to see what programming can really *do* for biology. As far as modelling goes, that happened on the side – I am still not entirely sure what they do. But, they seemed to produce some nice graphs, which show what we want. I seem to have forgotten all the maths I was ever taught somewhere in the last three years…"	**"**Both the diagrams and the differential equations that we use have simplicity at the heart of it. I mean we are talking about different genes and their relations to each other and so the obvious thing is to draw out that network onto a sheet of paper. And that is similar to electronics, apart from the fact that we don't have wires in synthetic biology."

These quotes reflect the partial understanding about work that went on in the 'other' discipline; there was a disjunction between biologists and those with engineering or physics backgrounds. Biologists were reluctant to do computer modelling – all the maths, circuit diagrams and graphs involved – and yet, they were fascinated and supportive of the fresh ideas and outputs that engineers and physicists were bringing. The engineers, on the other hand, found the amount of biology language far too onerous to learn in a short period; they wanted their colleagues to give them data that they could use, in a familiar fashion, to represent the systems, and, at best, make some predictions. During a memorable tea break with Alex and Chelsea, they described these caricatures:

- Alex is the "token engineer" – he likes to simplify and streamline problems and to number crunch; he wants to make models that can be used to build stuff; he's inclined to work by rules of thumb.
- Chelsea is the "token physicist" – she likes to make models too but she likes to actually represent the reality of a complex system; she doesn't like to make everything as simple as the engineers.
- The biologists of the team like to remind everyone how complicated biology is and how simple models won't work – they are always saying how this or that might be toxic to the cells, or that there is complexity in a pathway that models don't capture.

Although one can acquire a basic language of synthetic biology (the Cambridge crash course afforded this opportunity), it is quite a leap to call someone *a synthetic biologist*, in the sense that he / she might have all the knowledge necessary to design and carry out this line of work. Involving oneself in iGEM (and in the field more broadly) means learning how to utilize one's skills *in a team* effort, willing to be involved in an artful combination of individual knowledge and talents that are working towards a collective vision. The Cambridge team quickly recognized major talents and efficiently delegated – Emma, Derek, Eleonore and Senni were wet lab practitioners; Chelsea, Alex and Tobey were masterminds behind computer modelling and making the Wiki. In what could have been a much more difficult group dynamic, I was struck by how these characters made it work.

> There haven't been any major fights or disagreements at all. It has been a nice little group. I mean, we've all been stressed at different points, but there has never been an argument. – Eleonore

The advisors were impressed by how well this group worked together; although they lent support and helped when asked, as the summer progressed, students were increasingly able to get on with the tasks at hand and required less supervision. Still, Andy remained almost a constant presence as he worked on his PhD just down the hall from the team's lab; his attentiveness was invaluable as one of the rare practitioners who are versed in both engineering and biological aspects of synthetic biology (having worked in the field for over four years at that point). Douglas was also extremely helpful as he acquired tools and materials for the team and, like the other advisors, was a fount of knowledge on everything to do with microbiology. Samuel, Geoffrey and Frederick – the most senior and knowledgeable figures of the group – were around less often than Andy and Douglas, but nonetheless were always ready to provide additional advice. As the project developed, the team benefited from weekly meetings with at least a couple of the advisors to discuss general progress and troubleshoot problems.

Even though there was plenty of support and all the best equipment iGEMers could hope for,[93] the amount of freedom in this project remained greater than any individual on the team had experienced previously. As Andy said:

> The freedom that the group gets is really what can make or break them as researchers – they have a bunch of new skills to learn and nobody is spoon-feeding them. Students have to find out their own protocols and experiment with how to make things work! Plain and simple – there is a lot of doing your homework and a lot of trial and error.

[93] Cambridge University's excellent alumni relations in biotech companies, in part, helped Douglas secure team sponsorship and donations of equipment and biological materials (http://2009.igem.org/Team:Cambridge/Sponsors).

Several students echoed similar sentiments; Emma explained that her previous lab experience had always been "like following a recipe – you do these things, in this time frame, and if you don't get results, you'll be given some". She described iGEM work as "a huge trial by fire" – where making sure the lab was clean, ordering materials, setting up controls and refining or making new experimental protocols was all the responsibility of students. However, this curious, clever and dedicated group were equipped for the challenges at hand. Delegating tasks has already been mentioned, as has the group's tendency to surround their workspace with To Do lists and mind maps – these were certainly important organizing mechanisms.

Another essential aspect to the team's effectiveness relied on Emma's graceful leadership – noted in my observations and through comments from advisors and students. It was no surprise that Emma proved to be a brilliant conductor of this peer group – a top-student; an outgoing member of the rowing team; humble, yet vibrant (notorious for her 'happy dance' when good results were achieved in the laboratory). She was a fastidiously organized task master, yet sensitive and appreciative of the stresses and frustrations that all team members experienced. Emma was also efficient at getting to grips with new ideas and techniques. She remarked:

> Douglas would be speaking [about a modified technique or protocol] and I'd say to myself, 'OK, those are important things – I should write them down'. So then I've got some massive list and he just talks about it so easily because he's been doing it for years – and, for me, *every step is new*. I have to look at every one individually and figure out what is going on, but to him it is really quick. And now, I've gotten to the stage where – obviously not Douglas level – but, I can do a PCR without having to read books.

Samuel also commented, “Emma is just quick on the uptake every time”. It was required that all students get on with their work, write out protocols and devote a huge amount of time to learning new vocabulary, new materials and new skills; on top of that, Emma effortlessly took up the reins as a leader who drew over-arching maps (‘THE BIG IDEA’ diagrams), brought the group together to discuss what everyone was doing and managed to always know at least a little bit about every aspect of the project. Finally, Emma was also gracious to me, incredibly helpful in explaining laboratory work as I often ‘hung out’ alongside her.

Before moving on to discuss the practices and processes of this design and experiment stage, I’ll highlight one more story of an individual’s development. At the beginning of the summer, Senni was a second-year biochemistry undergraduate who had very little laboratory experience; by the end of the project, he had done something in the realm of fifty gene assemblies (advisors told me that this number would be a rare achievement for most grad-students or post-docs in three years!) and he had earned the endearing nickname, The Professor. His personal success story, however, started with a rare moment of tension that occurred in this group. Andy recalled this specific irritation with Senni:

> It was that one morning, you remember… Senni started pulling plates out; I don’t know where he was getting them from, and he had no idea what was what, and what cloning came from which line, and which graph was which graph, and where was his control. And it was probably the tenth time in that two weeks that I’d said, ‘where’s the control?’ and he’s like, ‘ooohhh...’

Andy added that, at that point, Senni requested his help on an experiment that he felt was a waste of time. They had insufficient materials, which meant a low likelihood of getting results and there were further doubts about the genetic construct that Senni intended to work on. Senni agreed that there was good reason

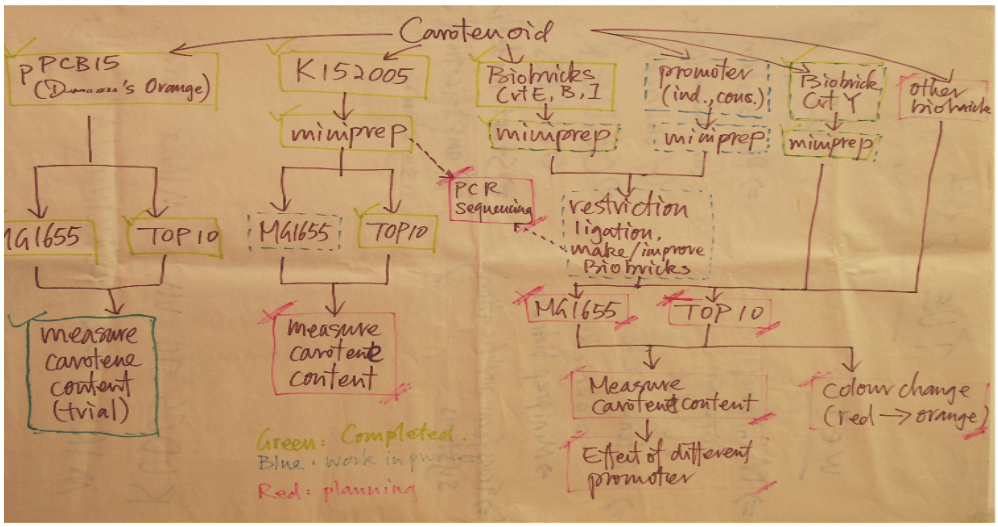
to be sceptical of the chance of that experiment working, and yet his persistent attitude was, “why not just give it a try!”

With stubborn determination and luck, Senni’s experiment worked the first time. He admitted to me, however, that at the project’s beginning, he didn’t have his controls organized. Lessons were learned:

> I got the hang of it… When something failed, we modified the protocol to make it better. It was much more encouraging. During the first few weeks, we were just very inexperienced – we hadn’t used the kits yet and we were just following the recipes and sometimes it doesn’t actually work... At first, we were quite cautious – you know, if the protocol says ‘1 minute’, we followed it for exactly 1 minute. But then, later, you realize what is more important and then you have the confidence to try out new things and explore new areas which will be able to bring the project forwards.

Senni *became* an excellent scientist, as he evolved and refined in his skills over the summer. Advisor Samuel explained Senni’s transformation, where he went from being “completely all over the place – you were just hoping to God that he wouldn’t destroy something in the lab” to “someone that actually did the controls in experiments, knew where all the data were, put things together in a sensible order so he could explain the results to anybody that came by – it was all logical!” Figure 4.3 illustrates some of the impeccable organization in Senni’s mapping out his work on the carotenoid pigments.

Figure 4.3: Senni's Carotenoid chart



During his personal development, Senni also made a concerted effort to extend a positive attitude towards his colleagues, making him not only a valuable team member in terms of churning out results, but also in terms of helping to foster an encouraging atmosphere:

> I like to work in the lab – especially when things are *working*. I mean, it is tiring. But, when you see things work and you see the whole team progressing – especially when Eleonore was able to make the violacein work in the liquid culture – it really makes it all worth it. Eleonore was able to bring the violacein into large amounts in liquid and then, I measured it and I saw a very good colour. And her colour is very distinct so I think very useful. Also, the amplifier project now has all the all the things in the correct system – so now the next step is to just put the parts together and just test them. I see it all moving forwards now. It is all worth it!

Positive attitudes in the team were essential in keeping the project moving. As Frederick reminded me, experiments are full of error and with high-achieving iGEMers, "there were definitely times of panic and unhappiness – tears on more than one occasion, and frustration, but then I think that's all very much par for the course".

Practices and processes

This section is an examination of practices and processes involved in the team's design and experiment phase: well-established wet laboratory protocols that often fail and require several repetitions are discussed; other work involves maths and computer modelling; the simple use of pen and paper to map ideas is illustrated further; finally, I describe the team's 'in silico' designing and ordering of a bespoke gene construct, as well as the arrival of the synthetic DNA (via post) and its insertion into living cells.[94] An important point about the setting is that all work was conducted in the same room – a simple laboratory space on the top floor of the Plant Sciences Department, overlooking a tidy green courtyard – separating two 'wet benches' from two 'dry benches' by posting signs at the end of the bench rows.

Biologists were the main work force in Cambridge's wet laboratory; only rarely did the engineers or physicist decide to conduct experiments, mostly preferring to keep to their computers. So what exactly did these biologists do? Despite the rhetoric associated with the field about modular, off-the-shelf components that fit together like Lego™, the vast majority of actually "*doing* synthetic biology is really about clear liquids and small volumes", as an engineering student remarked. In molecular biology experiments, Frederick repeatedly reminded the team, "most of the time stuff doesn't work – you just have to get used to that". The following table illustrates some of these common molecular biology procedures (which, crudely, is just repeated transferring, cooling, heating, adding, shaking and waiting for clear liquids and small volumes to do something). What the reader

[94] It is a huge luxury for an iGEM team to use synthesis technology, as it is considerably expensive. Cambridge's alumni connections at synthesis company, DNA 2.0, provided the team with £3000 worth of gene synthesis – for free.

should note in Figure 4.4 is not the technical detail, but rather, how these synthetic biology wet lab practices are rather mundane, tedious and, despite what is said to the contrary, these are *not new* biology protocols and they are executed much like following a recipe (over-and-over again). Figure 4.5's photographs also show the discrete nature of this kind of labour, something that remains highly reliant on the experimenter's excellent hand-eye coordination.

Figure 4.4: Example wet laboratory protocols[95]

Protocol	Details
Producing competent cells[96]	Starting from a single colony on a plate: • Transfer colony into 50ml liquid LB media and leave in a 200rpm shaking incubator overnight • Take 10ml of culture and inoculate into one litre LB and grow in shaking incubator until OD600 of 0.2-0.3 (4 hours?) • Put culture on ice for 30 minutes • Centrifuge at 4000g for 6 minutes • Remove supernatant and resuspend cells in an equal volume of ice-cold 0.1mM HEPES • Repeat centrifugation • Resuspend cells in 0.5 volume ice-cold 0.1mM HEPES • Repeat centrifugation • Resuspend cells in ice-cold 10% glycerol (20ml) • Combine to form two tubes of 40ml glycerol • Repeat centrifugation • Resuspend in ice-cold glycerol (3ml) • Divide cells into 100ul aliquots and store at -80 (Cells should be at a final volume of ~3 x 10^10 cells.ml^-1)
Competent cells transformation	• Electrocompetent cells thawed on ice • Prepare vector DNA on ice • BioBricks o With pipette tip, punch hole through foil cover into designated well o Add 20uL DIW o We will be removing about 5uL; the rest needs to go in an eppendorf, labelled with biobrick number, and stored at -20°C • Violacein and melanin need to be thawed • Vector DNA pipetted into chilled 1mm separation electrocuvette = 4 total • 5uL of BioBricks • 0.5uL of melanin and violacein plasmid • Add 45 uL competent cells • Tap electrocuvette gently to evenly spread mixture in the electrocuvette gap with no air bubbles • Thoroughly dry cuvette

[95] http://2009.igem.org/Team:Cambridge/Protocols.

[96] Making cells competent in the laboratory means preparing them so they are more permeable, ready to take up DNA that will be introduced into the environment later in experiment.

	• 1.68 kV passed across cuvette, 5.1-5.4 time constant at 200 ohms and 25 uF • Add 0.25 mL SOC liquid medium to electrocuvette • Incubate electrocuvettes at 37 degrees C for 60 minutes • Pipette 150uL onto a (warmed) selective LB agar plate, spread with blue spreader • Orange genes BioBrick: ampicillin • Promoter for orange genes BioBrick: ampicillin • Melanin: ampicillin, copper, and tyrosine • Violacein: trimethoprim • Do 1:10 dilution with SDW into a new eppendorf Pipette 150uL onto a selective LB agar plate, spread with blue spreader, 4 separate inoculums
PCR procedures	**For high accuracy sequence PCR** • Use the Phusion set from Finnzymes • 50ul solution • Can alter conditions for optimisation **For verification of plasmid presence/length** • Use TAQ polymerase and buffer from stores • 20ul solution • Run with standard procedure as follows for Colony PCR **Reaction Mixture** • Template: 1 uL from O/N culture (1-2 uL if colony picked straight from plate into water) • VF2: 1uL • VR: 1uL • Eco-Taq: 0.2 uL • 10X buffer: 5 uL • dNTPs: 0.4 uL (stock is 10 mM) • make up to 20 uL volume with H20 **Reaction procedure** • 95 degrees C for 2 minutes • 33 cycles of: • 95 degrees C for 30 seconds (denaturation) • 65 degrees C for 30 seconds (annealing) • 72 degrees C, 1000bp/min (elongation) • 72 degrees C for 5 minutes • hold at 4 degrees C **Gels** • Run on EtBr for good quality viewing (make agarose gel). This is viewed in the red-room downstairs. • Run on SYBR-safe gel if the DNA is required. This can be viewed under blue light in the covered dark-area.

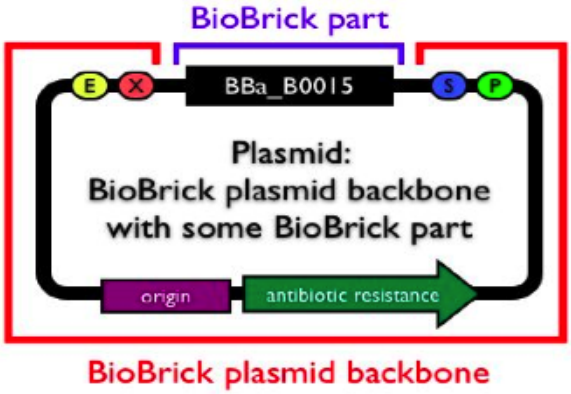
Figure 4.5: Wet work

Another essential protocol in iGEM is 'BioBricking' – that is, 'snapping together of DNA components', as the Lego™ parallel implies. A standard BioBrick is pictured in Figure 4.6 and consists of the following components: (i) a gene[97] (or small set of genes), that encodes a function and is given a standard name (this part is bracketed in blue, named BBa_B0015); (ii) a plasmid[98] (represented by the red bracket); (iii) prefix and suffix sections that contain restriction sites (the circles on either side of the gene), which are short flanking sequences around a gene that allow them to stick into a plasmid or to another gene; (iv) an origin of replication (the purple square) that allows the plasmid to be copied in a bacterial cell; and (v) an antibiotic resistance marker (in green) that allows the researcher a way to only work with the right bacteria that have taken up this whole plasmid + BioBrick format.[99] Using a process called standard assembly and a series of other well-established laboratory techniques (e.g. cloning and gel electrophoresis), BioBricks can be cut and pasted together and taken out or placed inside living bacterial

[97] Acquired from The Registry in standard BioBrick form, or removed from bacteria (and occasionally other kinds of organisms), or designed and ordered online.
[98] See Key terms, p. 10.
[99] Plasmids are put into bacteria in a process called transformation; then, bacteria are plated onto antibiotic plates so that only those with the antibiotic resistance (containing the plasmid + BioBrick construct) survive.

cells.[100] BioBricking is one of the most fundamental accomplishments for iGEM teams – to do well in the competition, teams must demonstrate a mastery of this protocol and, the most significant players, will have constructed a number of new BioBricks to give back to The Registry.

Figure 4.6: Standard BioBrick

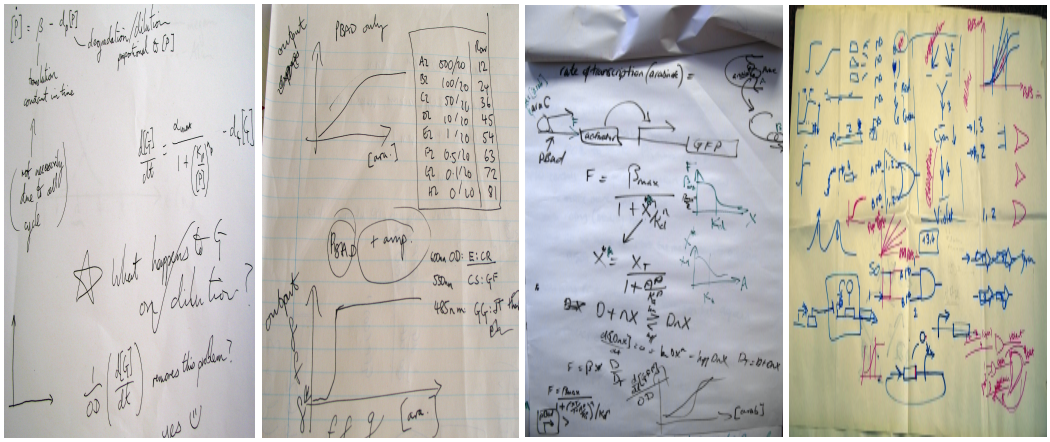


To illustrate some of the team's dry work, I must ask the reader to forgive the broad-stroke nature of the descriptions I offer about computer modelling as I've found this element of synthetic biology most challenging to comprehend and describe (given my limited mathematical and computational knowledge). The general aim of modelling in synthetic biology is to provide 'simple' mathematical frameworks that describe (and, at best, predict) the behaviour of engineered biological systems. The modeller's task, therefore, is to construct the 'Ordinary Differential Equations' (ODE's) and many sets of graphs that accord to their project's various system operations. Modelling can, for instance, say something about rates of change in reactions; it can utilize production-degradation equations; it can show how gene expression dynamics and signal transduction is operating; it

[100] See http://partsregistry.org/Assembly:Standard_assembly and 'Creating Biobricks' post (23 July 2009) on http://labrat.fieldofscience.com/.

can say something about concentrations of a chemical input that might be necessary to trigger a set of reactions or output. Modelling tries to find simplicity in a complex soup of noisy biological networks and does so by searching out defined structures, reusability or recurring patterns (network motifs), modularity ([input]-[processing]-[output]) and feedback loops that operate on regular timescales. There is also a necessary back-and-forth that involves using real data generated from wet laboratory experiments and feeding it into the mathematical models – the wet and dry protocols then continuously shape each other. For example, experimental samples are measured using a piece of laboratory equipment, a plate reader, which generates data about biological, chemical and physical characteristics of specimens under examination; this information is then fed into the mathematical and computer simulation models and fine tuning of both wet and dry work can proceed. Leaving this modelling overview, in the next chapter the reader will find illustrations that show selected final outputs of this work. Until there was actual wet lab data to work with, modellers typically continued to map out ideas of how models *might* work, with *theoretical* data (Figure 4.7).

Figure 4.7: Mind mapping from modellers

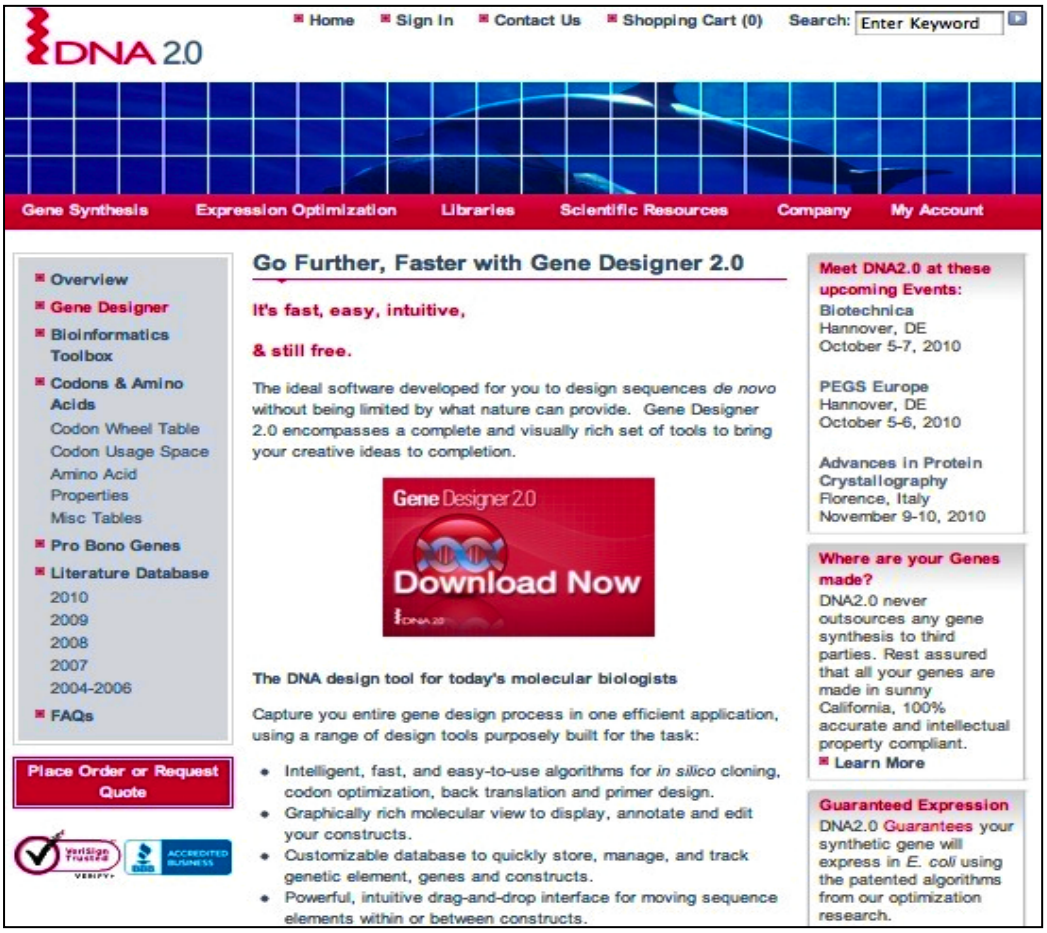


Finally, the most cutting edge practice that the team employed was in Eleonore's work on a bespoke design to make violacein, a purple pigment found in marine bacteria. Through research, Eleonore found that there exists five genes in this system (labelled in Figure 4.8b as vioA-E) that, when working together inside a bacterial cell, could produce a violet pigment. She also found that there exists at least one (if not two) intermediate(s) in the genetic pathway that might allow the production of a blue or green pigment, if certain genetic components were knocked out or rendered inactive. The exciting prospect of a two (possibly three)-in-one system, producing multiple colours convinced the team and advisors that this would be an area of the project worth spending extra time and resources on. It was decided that Eleonore could use the free DNA synthesis that the team had been given by DNA 2.0 in order to create the ideal violacein genetic system.

To begin this process of designing, ordering and experimenting with synthetic DNA, Eleonore worked on DNA 2.0's free software, Gene Designer 2.0[101], that allows users to input and manipulate genetic code in silico in order to optimize a desired sequence before ordering it (Figure 4.8a).

[101] https://www.dna20.com/genedesigner2/.

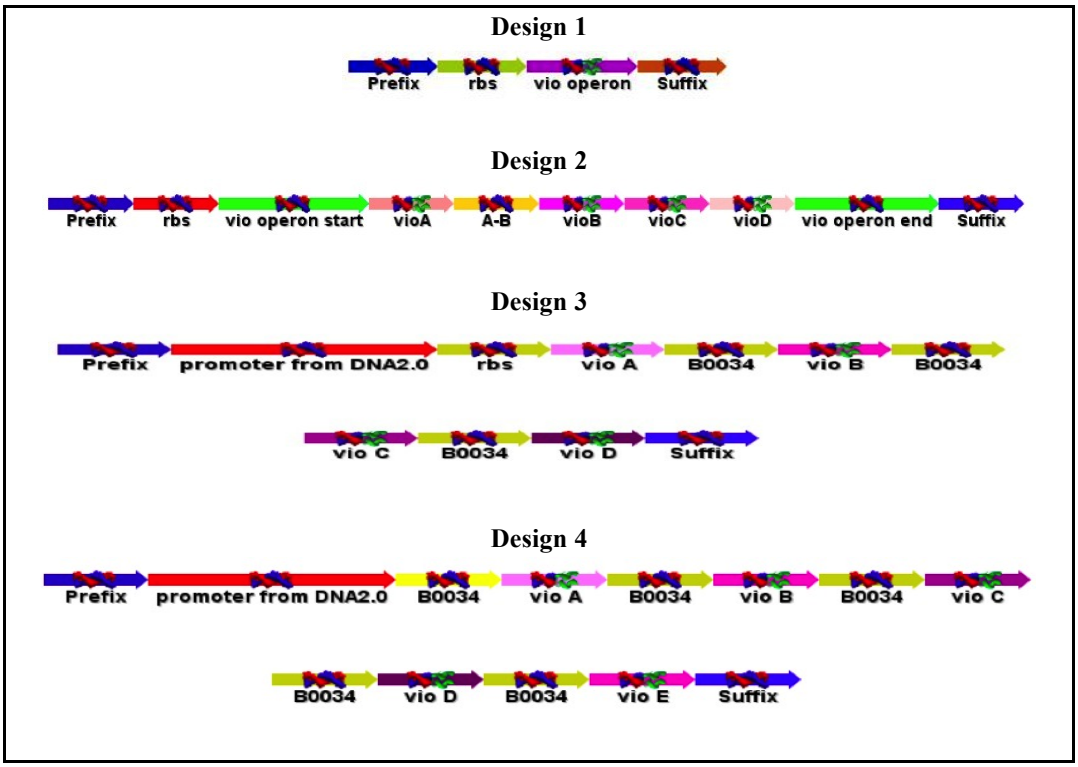
Figure 4.8a: Design and order your gene online!



The program shows DNA that is broken down into modular, functional pieces and represented as arrows (4.8b), though it can also be looked at in sequence form, showing, for instance, what proteins are made from a given component and where cuts in the DNA can be made (at restriction sites). Four iterations of Eleonore's design are shown below, though she had saved "about a hundred incarnations" on her computer. She started simply, with just the vio operon (the five genes, one after the other), surrounded by the BioBrick prefix and suffix. After examining the operon in greater detail, Eleonore realized that some bits of the genetic sequence were out of sync, and producing undesirable (or, apparently non-functional) amino acids. She then carefully planned removal of non-functional DNA and mapped out all the useful nucleotides so they were lined up to optimally make the

desired proteins (which would ideally produce the desired pigments). Eleonore also added standard parts to her designs that were meant to improve protein yields. Designing this kind of construct in silico necessitates a thorough understanding of the biology (in broad terms as well as specifically in the genetic system that is being engineered) in order to judge what might make the system work better, be it through the addition or removal of segments of DNA.

Figure 4.8b: Evolution of a gene design



Modified from 'Stages of Design' post (12 August 2009): http://labrat.fieldofscience.com/.

Upon completing the design online (a process which involved a great deal more thought than I describe here), it was as easy as sending the code attached in an email and waiting for DNA 2.0 to synthesize. The team's bespoke violacein sequence arrived by courier a few weeks later. Then, the experiments with this novel construct commenced. After one unsuccessful attempt, this specially

tailored sequence was transformed into live *E. coli* cells. A few rounds of microbiology experiments later – chopping and changing parts of this construct – Eleonore had this synthetic system producing violet and green pigments. Further results details are found in the next chapter. Understanding the evolution of the project ideas, the team dynamics, as well as the experimental practices in the Cambridge team, I turn to discuss the Imperial College group's mid-project developments.

4.2 Evolving ideas at Imperial College

The project develops

After the team decided to attempt creating drug-producing, self-encapsulating bacteria, there remained several steps to fully formulating the project before experiments could begin. One major (somewhat stalling) point was deciding which application the group would gear their project toward. Several possibilities were researched, including providing treatments to lactose intolerance, Gaucher's disease, cancer, cystic fibrosis and glycogen storage disease (Andersen's disease). With each potential application for a given ailment, students worked out a basic understanding of biochemical deficiencies; they considered 'compelling' messages that could be coupled to the project; they worked out a hypothetical drug intervention; and they examined feasibility. I should emphasize that the project was recognized as having rather lofty ambitions; students knew they would only be able to construct a fraction of the overall project and there was no realistic possibility of them actually constructing a drug-producing *E. coli* for human consumption. As the team chose to focus more on an exciting project vision, they sometimes made quite creative. For example, one student found a

study showing that anthocyanin prevents oesophageal tumours in rats, as well as colon cancer; the grand hypothesis that followed this finding was that if the team could synthesize this compound, they might be able to pitch their project as a cancer treatment.

Deciding how to narrow down the project's applications and refine the engineering approach was largely driven by early comments from head professors. At one point, Bernard suggested that "children and disease is good… working to solve AIDS in Africa or curing cancer – this is the stuff that appeals to a Western consciousness… the stuff that wins"; he also commented that students shouldn't hesitate to put pictures of suffering children in their presentation, if applicable. Joking aspect of this comment aside, it was odd to encourage this kind of fantasising to a team of aspiring practitioners of biotechnology. There were a few cringing expressions during that meeting. Beyond advising the students to focus on one or two captivating applications, the professors also stressed showing modularity in the work so it looked like a manufacturing platform where many possible drugs could be made. They had to seek out something prize worthy. Furthermore, it was advised that each module should be represented in engineering terms – with plenty of computer models, data and maths. Roger also emphasized that students ought to show "quality control before consumption", as people might dislike the idea of consuming their medications with a genetically engineered bacteria – the obvious fear being that the bacteria could interact harmfully inside the human body, or multiply out of control.

With each day spent researching and debating the project in theory, pressure to get started on something in reality mounted. After three weeks of tireless work (days, evenings and weekends), the team outlined their (*hypothetical*) emotive and engineering-driven project, paraphrased here (and visualized in Figure 4.9):

- *The project:* Auto-encapsulation of protein drugs for release in the small intestine.
- *Applications of focus:*
    - *Treatment for Phenylketonuria (PKU) disease:* PKU is a genetic metabolic disorder, characterised by a deficiency in phenylalanine hydroxylase (PAH), the enzyme needed to metabolise phenylalanine. When phenylalanine is not properly metabolised, its build up causes problems with brain development, leading to mental impairment and seizures. There is no cure for PKU; its negative effects are reduced by special diet alone (low in proteins and starch). The diet, however, is unpleasant and decreases quality of life for PKU sufferers, particularly children and teenagers. The team aims to develop an application that would allow PKU sufferers to eat a normal diet by delivering PAH enzyme to the gut (in the form of an encapsulated, microbiologically produced drug) to break down phenylalanine before absorption.
    - *Engineering cellulase to "help end world hunger":* Humans lack endogenous enzymes to digest cellulose. However, if we were able to metabolise plant cellulose, it could be nutritionally beneficial to a human diet – not only providing dietary fibre, but also nutrients and calories. The team aims to develop an application that would

deliver the cellulase enzyme to the gut, which would allow higher calorific and nutritional output from plant consumption. Arguably, students remarked, this project could "help end world hunger". ("Just imagine if you could eat wood!" exclaimed one student.)

- *Demonstrating modularity (an interchangeable, multi-purpose drug-manufacturing platform) through defined stages:*
  i. *Cell growth:* Cells grow to a critical density before the system starts.
     - *Chemoinduction:* The addition of IPTG (a common molecular biology reagent) kick starts the system once cell culture has reached sufficient density.
  ii. *Module 1 – Protein production:* Produce a protein of interest.
     - *Autoinduction:* The cell culture has two carbon sources for consumption. Once the primary source (glucose) has been exhausted, the system switches to metabolise the secondary carbon source; this switch triggers commencement of the next module, encapsulation. Furthermore, adjusting initial concentrations of each carbon source affords a programmable time delay between Modules 1 and 2.
  iii. *Module 2 – Encapsulation:* After producing the protein of interest, the cell is triggered to produce colonic acid, which coats the bacterium and protects it from acid degradation in the stomach.[102]
     - *Thermoinduction:* The system is initially grown at 28 degrees C, at which point Module 3 is repressed. Upon increasing temperature to

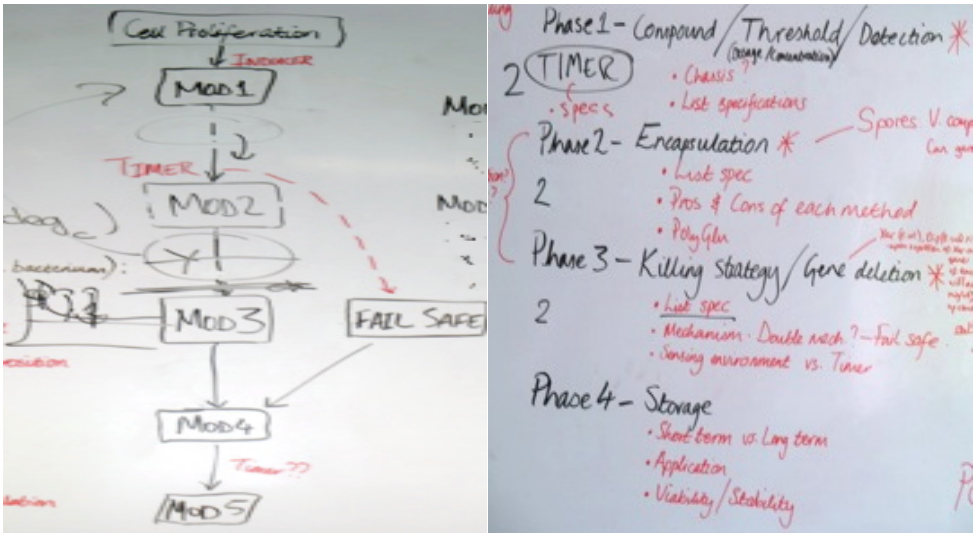
[102] Note that during the first few weeks, while researching various applications, the group considered another kind of coating, alginate. However, this route was found to be far too complex, as it would necessitate building at least a six-gene construct.

42 degrees C, repression is blocked and Module 3 is activated.

iv. *Module 3 – Genome deletion:* Once the cell contains the protein and is encapsulated, this module triggers over-expression of restriction enzymes that cut up DNA, thereby killing the bacterium.

- *Secondary encapsulation:* Hypothetically, the generated material would be encapsulated again and manufactured into tablet form, ready for consumption. (For obvious reasons – cost, lack of time and equipment, health and safety, etc. – the team did not plan to do this for iGEM.)

Figure 4.9: Mapping out the project vision



Within this clearly outlined project, there were logical sections to be drilled down in specific detail. Two engineers and a biochemistry student proceeded to work on several models for a timer and the switches (chemoinduction, autoinduction and thermoinduction), while biologists mapped out which genes would be required to produce compounds of interest, allow for the bacterial encapsulation and initiate

"cell suicide".[103] The biologists also had plenty of background research to do in terms of understanding quality control variables: they needed to know information about pH and other conditions of the human GI tract; they needed to explore unintended effects that this drug-production method might lead to; they needed a good idea of how the genetic components they would use function, so that they could attempt to build a hypothesis about safely designing this system's interaction with complex human bodies. Obviously, students could not look into all possible considerations of their project, virtually an endless task when considering a human intervention; however, as advised, the team was demonstrating a concerted effort to investigate and integrate finer details into their project that they hoped would look impressive at the competition.

The Imperial College team didn't go into the wet laboratory until a comprehensive vision of their system had been constructed (unlike the Cambridge team where experiments were underway early, while the project ideas evolved). They were also waiting on certain components for the project, such as genes requested from other academics or ordered through a DNA synthesis company. This postponing of hands-on experimental work meant the team did a great deal of planning out protocols along with further developing ideas in the dry lab, such as making a timer. However, making the designs more intricate turned out to be time wasted when, in week five, the senior advisors rejected the complex plans in favour of a simpler approach.

> Go for simple design. Do not go for complicated – it won't add anything to the project… What will improve our position in the competition are data and some functioning parts. It is not about over-

[103] I won't go into more technical detail. Note that, as with the Cambridge team, genes were taken from The Registry, ordered from a DNA synthesis company and requested from other academic laboratories. For further, see: http://2009.igem.org/Team:Imperial_College_London/Wetlab.

> complicating and tweaking at the moment; it is about the basics. – Roger

Even though dry work proceeded to some extent (with theoretical models and data), and wet laboratory prep was done (e.g. competent cell strains were prepared for future experiments), not gathering data from real experiments until after week six was a significant hold-up. Looking back at that stage, Matt commented:

> We had a meeting with the professors and it was basically the end of week six and they just asked what we were realistically going to be able to do. So, we looked at all our assays… and we said, 'OK, we're going to look at one gene from Module one; we are going to look at encapsulation because that is the most important part of or project; trehelose is not really going to – well, it was a bit of an extra, it would be nice if we got it but probably we probably weren't; and Module three we can sort of get what we can'. So that was quite important because, in our minds, it put us all on track in terms of what we were going to be able to achieve in the short time we had left. *This signalled going from theoretical to practical.*

From the project's start, I mentioned my willingness to help the team with a human practices side project, as the competition's website clearly stated that this would be considered in judging the projects. It was encouraged that iGEM students address synthetic biology's broader issues in public engagement, intellectual property, safety and security, as applicable to their projects. Given my familiarity with such topics, I was well placed to help the students do something meaningful in this regard. Moreover, I felt that this is could be a valuable component to the iGEM learning experience and I wanted to offer a gesture of thanks for all that I had been taught by the team. There was mixed support for taking on this work and despite there having been ample time to start building a human practices project early on, it was set aside as something the team would get around to later. As later in the project approached, support for doing a human

practices section seemed to wane – students and advisors alike were stressed about getting the "real work" done, with Zach, for instance, remarking that "any moment not spent in the lab is a moment wasted". A few students also filled me in on what was said in meetings that I could not attend. Second-hand, I'd heard that Bernard said he didn't understand the point of doing an ethics project; John, however, was more encouraging and thought it was a good thing to do if it didn't take much time. The human practices project was also competing for time that some thought would be better spent not only in the lab, but also on improving the Wiki, building the presentation, getting the poster started and designing team T-shirts.

Still, there was enough enthusiasm with a couple of students (especially Andrew) and a couple of advisors that we were able to go ahead with an "ethics side project" in week eight. Before explaining how the ideas for this section of the project evolved, it should be noted that the group also had a one-day workshop with a designer that occurred earlier in the project. On that day, students were encouraged to engage with broader implications of synthetic biology by imagining possible futures for the field, once applications hit the mainstream. Although this one-off exercise was creative and fun for the team – as they clipped through newspapers and magazines and made artful poster presentations that constructed hypothetical timelines for synthetic biology's future – the idea of actually incorporating critical design in the project to think about social and ethical issues did not significantly materialize.[104]

[104] The reader will see in the next chapter that, at Cambridge, the inclusion of critical design perspectives became integral to their project.

When Andrew and I finally found time to think about the human practices project, we brainstormed (as the rest of the group continued with other tasks at hand), talked through goals and set out a specific plan for how to achieve them in a timely manner. Andrew expressed that he really believed that having a human practices project would help the team win a prize at the competition, and, more profoundly, he wanted to "provoke a change in how people view the project". He had been reading through an old philosophy text he studied during his International Baccalaureate – Andrew pointed out quotes from Pascal, Sartre, Hobbes and Nietzsche, describing to me his interests in questions such as 'what is the meaning of existence?'; 'is scientific knowledge *factual*?'; and 'what is the universal value in humanity?'; as well as his curiosity in Kuhn's theory of scientific revolutions or Popper's concept of falsification. Andrew also explained that he had a friend who studied philosophy, with whom he enjoyed regularly talking about bioethics. The friends had co-written a couple of articles, including one that described the potential of biotechnology to "sow the seeds of our own destruction".[105] Andrew clearly had a deep curiosity in philosophy and sociology of science, and a desire to do "something more than just throw around the buzzwords" (i.e. biosafety, IP and biosecurity with respect to synthetic biology). However, we both recognized the team's pragmatic priorities and were mindful not to add much more to the already lengthy To Do list. After two general discussions and one meeting with the whole group,[106] we outlined a plan: I would

[105] Andrew gave me a copy of this article, evocatively entitled, 'I have a gene, that one day…'. The article considered issues of human enhancement as well as social and political conflicts that may arise across developed and under-developed countries as a result of 'the biological revolution'. It concluded: "the key to safely undergo this major turn is scientific and social critical debate… [to] permit society to sow the seeds of responsible change as opposed to those of human destruction".

[106] This meeting generated a couple of interesting, if not bizarre comments. One student suggested we get an anti-GM activist to debate with the team on film; another student suggested the team go Speaker's Corner to try to generate a public discussion. This latter idea was quickly snapped back

run a morning workshop to stimulate discussion on various commonly depicted social and ethical issues in synthetic biology; I would then interview each student, loosely talking around three themes (described below) and this would be video-recorded. The video footage would then be cut down and used in the team's Wiki and at the Jamboree; finally, Andrew and I would produce some written work to describe what had been learnt in this team's human practices exercise. The three areas explored in interview were:

(i) *Describing the project in lay terms* – Andrew and I decided that an important challenge for iGEMers to meet was to be able to present their work in a publicly accessible fashion.

(ii) *Reflecting on the nature of materials used* – Discussing this subject was meant to provoke students to think about and articulate how they felt about being the creators of new biological forms. Did students believe that there was any special nature to these materials of 'life itself' or were they just another laboratory reagent?

(iii) *Risks* – This topic was meant to get students thinking about the risks particular to their project and how they might be mitigated.

The human practices work is further discussed in later chapters. Now that the reader understands how the project vision had developed as the group proceeded into the design and experiment, I turn to explore the evolution of team dynamics.

The team evolves

As an ambitious group, there were a few minor interpersonal struggles as students competed to have their individual visions achieved. Still, on the whole, the team

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at by Pierre: 'don't expect to go to Speaker's Corner unless you want to deal with some Hamas group of fundamentalists or other religious fanatics!'

got along well, appreciated that every person was crucial to the group's overall success and an increasingly friendly atmosphere developed. That's not to say that they did not experience a collective elevation of stress as time ticked on. Five weeks into the project, the team had only just started wet laboratory work and an anxious depression descended on the group – amongst students, mid-level advisors and professors alike. At the beginning of a team meeting around this mid-way point, Roger remarked disappointedly, "Is it Friday the 13th?" and Andrew admitted, "The project just isn't going fast enough". That meeting became one of a few sessions that addressed built up emotions and attempted to get the team back into gear; here, a few excerpts illustrate this session's tone:

> We're at least a week behind on the wet lab and on the BioBricks! – Max
>
> It is very hard to balance what quality the team wants to achieve with moving forward with the ideas and the lab work… – Kajan
>
> You [students] are not listening to our [advisors'] points! – Olivia
>
> Sometimes people are hiding a bit when they don't know what is going on in the biology. But people need to learn from each other and voice when they need help. – Andrew
>
> If we continue like this, we just aren't going to do anything. What are the reasons behind us not getting where we should be? … We are a team – we sink or win together! This is really starting to get annoying… – Roger
>
> If you go into the final, you will be presenting in front of a thousand people. You need to have personal pride in this project. A half-assed job is not good enough, not for what we're after. – John
>
> The mid-way phase of iGEM is very hard. It is difficult to see your way through the number of difficulties coming up. But, the key thing is to keep it moving and do so as a team. This is a competition – this is not just research! … You need to pull yourselves together and dig deep! … Do you really want to win this competition? Do you want to make an impact? How important is that? Because if not, you might as well bugger off. – Roger

At this same meeting, advisors declared that they would need to know who would commit to working beyond the initial obligation of ten weeks – it was expected that this would be everyone. In order to get the project to a competitive level, it was decided that students would have to accept that they'd be working right up until the Jamboree in the last weekend of October (this meant no holidays and working in any spare time once the academic term commenced in late September). Some students were whole-heartedly committed to making the best possible project and wanted to push ahead full steam, while others felt a little annoyed that they would have "no summer", spending the best part of four months fully devoted to iGEM. Advisors wanted the students to show more determination and respect for their advice, while students felt frustrated by the lofty and critical comments that Bernard and Roger tended to make when they were quite removed from the team's day-to-day actions. The stakes got higher as the competition finale drew nearer and I was very aware of being sensitive to the team's stress, often taking up more of an observer role, rather than a participatory one.

The group reasoned, similarly to the Cambridge team, that delegation of specific tasks to individuals (or pairs) on a weekly and daily basis was the best strategy to propel the work forward. After a slow start in nailing the project down, at week six, the team began to separate into the dry and wet laboratory bases – inconveniently on opposite sides of campus. Although students at Imperial College expressed the same kind of technical language barrier difficulty that Cambridge students struggled with, there was more mixing of disciplinary backgrounds over the iGEM months for this group. There were typically two to four students who worked on modelling: Nisha, with her bioengineering

background; Soo, with her engineering background; Kajan also did some modelling work, though he was new to it (coming from biochemistry); Andrew did some dry work too (he too comes from a biological sciences background). Zach and Felicity (both with biological sciences backgrounds) led the wet laboratory and were also joined by Matt and Sita (both from bioengineering and new to wet work); Kajan and Andrew also worked periodically in the wet lab, especially towards the project's end. On the challenge of working in a new discipline and the importance of perseverance and collaboration, Sita remarked:

> From an engineering point of view, it was quite hard to firstly get into reading these biology papers and understand them to the point where we could say, 'OK, we could modify this or that…' But then once you've looked at different journals and stuff online, you've kind of trained yourself up to learn the kind of things you're looking for. Also, input from others is critical. It was key to bounce ideas off everyone.

My relationship with certain team members also developed. I spent a good deal of time with Nisha and Soo, who made an effort to help me understand some of the computer modelling. I was impressed by Nisha's leadership and teaching skill, as she was incredibly patient with my slow learning process. Nisha and I had a friendly connection, talking outside the context of iGEM too about her interests in neuroscience, her travels and future ambitions. I also bonded with Andrew more than some of the other students, owing to his involvement with the human practices project and interest in my work. My relationship with other students was friendly and relaxed; I was grateful that, despite the obvious stresses, everyone made an effort to explain to me their work when it was convenient (something I judged carefully). Luckily, in biology, there are always waiting periods – waiting for the results of one step of an experiment before proceeding to the next – so, when in the wet laboratory, I tended to interject especially at these moments.

Gradually, my working rapport with Max and Pierre improved and they were usually generous with their time spent talking with me. Max was accommodating about what was going on in the wet laboratory, explaining experimental workings in understandable terms and periodically discussing synthetic biology's broader field gossip. With Pierre, his initial distaste for my social sciences work occasionally broke down, for instance, when we discussed parallels between economic and biological modelling. As time went on, I was also developing a certain robustness as a researcher – even when Pierre continued to roll his eyes at the social scientist's opinions (for instance, during the human practices workshop), it troubled me less and less. Besides, Pierre had shown a tendency to roll his eyes at most people, at one time or another. The other, more senior advisors – John, Bernard and Roger – were not involved in much day-to-day work of the team and when everyone did get together for meetings, the focus was on exactly what progress the students had made and setting out expectations for what was to come. Aside from the very early stages of my work at Imperial College, it wasn't until during and after the Jamboree that I had much chance at casual conversations with these participants. Overall, I had a more distanced set of relationships at Imperial College than I did at Cambridge. Nevertheless, good working connections were achieved and now, with hindsight, having a comparison of field locations affords a deep appreciation of how specific individuals and institutional cultures really shape ethnographic research findings. With the background of how ideas and team dynamic evolved, I finally turn to detail some of this team's design and experimental practices and processes.

Figure 4.10: Separate dry and wet laboratories

In the wet laboratory, much of the work involved routine activities that are described earlier in this chapter (with respect to Cambridge's practices and processes), so I won't belabour another explanation (Figure 4.4, the BioBricking process and online ordering of synthetic DNA[107]). Most notably, the team's middle weeks involved a progressive scaling back of expectations about what could be achieved in each project module, as biological complexities were confronted at seemingly every intended step. Olivia and Max assisted students in the wet lab, and their commitment was crucial in keeping the team going, despite a long haul of unsuccessful experiments. Olivia explained that typically, she or Max would go through experiments with students two to three times, patiently trying to work through possible problems; however, she also noted that "at a certain point, it can just be a huge waste of time and money" and so occasionally her or Max did procedures themselves.

Max commented that students were "pretty good" at building procedures (e.g. BioBricking) where they were "applying the rules and carrying on"; however,

[107] The Imperial College team's online-ordered synthetic DNA was significantly smaller scale than the Cambridge team.

testing procedures were more challenging, where there are many additional variables and "it can take a lot of de-bugging". The reality of several experiments was that it had been "tricky to try to get the bacteria to behave how we'd expect". Only one week prior to the competition, Max still felt that the team was at a key stage, without much data at all, striving to show proof of principle in each module:

> They've got it all laid out but they just need time now to test it. So, we've got the next week before the Jamboree. It is almost the most exciting part of the project – right before the Jamboree… to get the results is the most important part of the project. I mean last year, the most key result was got the day before we flew. So today could be a very important day – this RCSB, the encapsulation part, is the most important part of all of it. So fingers crossed, hopefully it will work.

The team was late in acquiring results – constantly faced with a biology that resisted their engineering attempts – and the majority of wet lab time was spent setting up, and re-setting experiments. Still, in the next chapter, the reader finds details of the team's results, acquired just in the nick of time. The photos below illustrate some typical laboratory practices.

Figure 4.11: Scenes from the wet laboratory

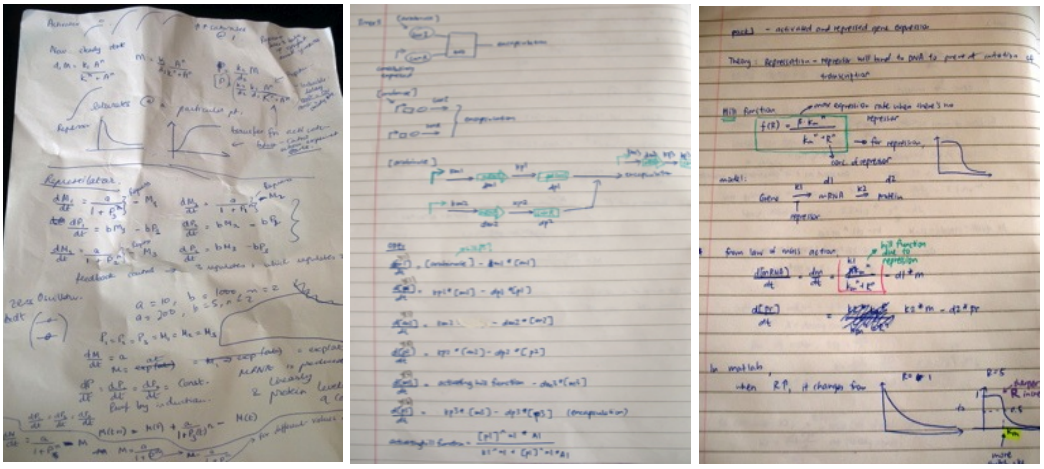
The team's neatly labelled DNA; plates on the bench; mixing and pipetting.

Moving to the dry lab, note again that the following chapter details models in their final form, with completed mathematical equations and graphs describing rates of change (even if only hypothetical proofs of concept). Throughout August, modellers focused on developing the mathematics that might simulate the transition stages of their overall project vision – the auto-induction, chemical induction and thermo-induction – and they also did a bit of theoretical work on enzyme kinetics. Figure 4.12 illustrates how this process began, similarly to the Cambridge team, by roughly sketching out equations and corresponding graphs that they might expect biological experiments to yield. Because of a long delay in acquiring any results from the wet laboratory, the students often did "plug and play" – inputting hypothetical values into their equations, yielding hypothetical graphs and computer simulations, rather than using real data.

> In a way, the modelling was trying to compliment some of the things that we didn't really get to do in the wet lab. But, then again, it is always better to kind of refine things later on so it didn't quite get there because there were sides of the project that were still missing...
> – Nisha

Everyone felt a bit in limbo until quite late in the project when, literally just days before the competition, there were some wet lab results to work with.

Table 4.12: From modellers' notebooks



For the human practices project, I began the workshop with a few provocative video clips from an interesting, if not hyperbolic and biased, BBC documentary which dramatically claimed that with synthetic biology, "scientists are close to repeating what has happened only once in four billion years – the creation of a new life form".[108] The students and Pierre attended the workshop and, though I was disappointed that the advisors showed little support for this event, the small group led to a relaxed and conversational workshop, with students leading discussion, while I periodically interjected to raise questions:

- What might broader publics think of synthetic biology? Should scientists be responsible for doing public engagement? Who is accountable for explaining this field to lay audiences – scientists, policy makers, social scientists, private companies hired to do public opinion surveys? Are there any foreseeable problems with engaging in a public debate about synthetic biology?

[108] 'The Spark of Life', an episode in a series entitled *The Cell* was aired on BBC Four (26 August 2009): http://www.bbc.co.uk/programmes/b00mbvfh.

- Is it at all unsettling that synthetic biology seeks to engineer life anew, for human purposes? Does this field's development really imply a "second genesis", as the documentary suggested?
- What are the risks in synthetic biology, broadly and specifically in the team's project? Who is responsible for governing the field?

Though I understood that having this group talk would influence students' responses in interviews that I conducted later that afternoon, Andrew felt that some team members wouldn't know what to say without having had a collective discussion about the human practices themes. Although I disagreed in some sense, as this was intended to be an exercise of the students' design, I followed Andrew's suggestion. All eight interviews were completed, back-to-back, taking no more than 30 minutes of most of the students' time (and ending in my exhaustion). A few days later, I enrolled in a workshop and learned to edit video. I then spent time turning over four hours of footage into a 30-minute cut of thematic interview clips for the students to reflect upon and use. The next chapter describes some interview highlights, as well as two documents that Andrew and I put together; further interesting plot twists with this aspect of the project are detailed in later chapters.

Conclusion

This chapter has captured some of the many challenges, practices, protocols, team dynamics and idea evolutions that both groups experienced during their design and experiment phase. There is, of course, overlap between this phase and the earlier stage of dreaming up ideas, as there is also overlap with moments of experimental success that yielded material results (next chapter). Previously, I

have shown the ways in which students utilized intellectual technologies (from mind mapping to computer forums) in order to dream up ideas, as well as described certain personalities and a different set of institutional cultures; these themes continued to be important in this chapter. Yet, in observing ideas turn into wet and dry laboratory practices, a number of additional conclusions arise:

- Synthetic biology, as taught and practiced through iGEM, entails a conflicting understanding of biology as both discretely engineerable and impenetrably complex. Nowhere is this tension more apparent than in the transition between *synthetic biology as a way of thinking* to *synthetic biology as a way of doing*.
- Synthetic biology, in practice, is far from a merging of biology and engineering; rather, it is about finding an effective way for biologists and engineers to work together, through different language barrier issues and visions of what might be possible.
- A successful iGEM project requires a team dynamic that supports getting through the many challenges facing iGEMers.
- Even in two seemingly similar institutions there are significantly different views on how synthetic biology ought to be practiced and performed in this competitive context.

In its ideal conception, synthetic biology is described as the creative coming together of synthesis, sequencing and computational technologies, under a *true engineering*[109] framework applied to biology; it is a field that brings modularity and physical standards to genes and microbiology so that, with grand functional

[109] This claim is often made and opposed to earlier decades of "genetic engineering" that saw ad hoc methodology and a limited scope ("just chopping and changing one or two genes").

visions, biological machines can be designed and built, only restricted by the imaginative capacities of its practitioners. However, this chapter has demonstrated that when it comes to actually getting ideas of a synthetic biological system off the ground, a process of *simplifying* the goals to what is achievable is of utmost importance. Most ideas that students are encouraged to dream up when armed with synthetic biology ideals are not even remotely possible experimentally because of a vast array of (known and unknown) biological complexities that resist being (re-)engineered. Specific to iGEMers, Pierre commented:

> They've got very little experience… They can't criticize what's on paper and they think that everything is reproducible – which is definitely not true in the case of biology. So they start building up grand ideas about, 'we can put this together and that together and if you put two and two together, you'll get four, five and six…' But the bottom line is you are not even sure you've got the two, let alone that two and two put together will give you six – three, at best! When you are very lucky. And that is probably what they discover over the summer, which is that *you probably cannot trust what is printed*. Experiments are incredibly difficult, unreliable and full of surprises. Basically, what you've started with – your grand idea – after a month, you realise that, well, it might not work that well... iGEM is a very ambitious project, but it is also very short.

Note something interesting here – the initial messages in iGEM teaching and promotion of synthetic biology ideals are misleading, and experienced advisors clearly acknowledge this. Frederick of Cambridge added that iGEM advisors always have a good deal of comforting to do, when students inevitably realize that synthetic biology is not yet what it wishes to be – every year, he claimed to tell students, "it's OK, it's not necessarily you; it may just be that the molecules don't want to do that and that's the way it goes". Yet, for a lucky few, successful experiments – such as Cambridge's design, engineering and implementation of the violacein construct in living cells – keep the iGEM competition celebrating synthetic biology's grand potential.

Another popular statement – that synthetic biology is a "merging of engineering and biology" – is worth deflating a little. In practice, this field really involves different disciplinary perspectives finding a way to their appropriate tasks for a given project. Although there were a couple brave students attempting true interdisciplinarity at Imperial College, my dominant observation was that engineers and biologists tended to prefer sticking to their own backgrounds – to either be fascinated with biological systems, or to programme and develop maths for systems dynamics in order to optimize engineering. They don't understand each other's languages: biologists may have a resourceful explanation for a given system's functional complexities; engineers want good data that they can "crunch" in order to produce models, graphs and predictions.

Interestingly, I might add that when Eleonore – the committed, self-identifying *biologist*, *not synthetic biologist* – was working on the violacein construct, she expressed considerable distress about a kind of disrespect for the natural order of things in this outsourcing, re-designing and re-engineering process of making synthetic DNA:

> I was a bit worried because I've always had this kind of non-synthetic biological view that the gene must not be messed with… If there are bits in there that don't seem to be doing anything, they *probably are doing something*, and we were just cutting those bits out, choosing to have only the protein coding regions, one after the other… Then we codon optimized it, and I did a bit of that myself but a lot was done on DNA 2.0's programme… And that felt wrong – actually going around and changing bases… I was thinking, 'what the hell am I doing to this genetic code – this is not going to work?!' … It felt weird, I'd be thinking, 'this gene should know what it's doing by now'[110]… But it makes sense, because when a bacteria makes colour, it doesn't want to do it optimally, because that would probably kill it – it would take

[110] Alluding to evolution's natural work.

> away too many metabolic resources to create too much pigment… so it is beneficial for the bacteria to use worse codons [in nature].

How biologists and engineers differently qualify and appreciate synthetic biology will arise again in later chapters.

I have also begun to demonstrate the importance of positive team dynamics and leadership. iGEMers face a long haul of re-evaluating and scaling-back initial "Big [dreamy] Ideas", an extremely steep learning curve and months of committed intensive work – not to mention lessons in dealing with criticism from themselves, peers and superiors. Pierre, with his usual cynicism, remarked, "iGEM is basically about projects that are born to fail" and "as a general rule, iGEM students have never really failed before – they are bright students who have always done well in their studies". To a large extent, this experience becomes about personal growth and developing group work skills. I've highlighted some examples in this vein – Emma and Senni's evolving roles on the Cambridge team, as well as Andrew and Nisha's roles at Imperial College as particularly strong leaders with open minded attitudes. Note Geoffrey's comment here on the necessity of leadership in iGEM:

> I was very impressed by the way some team members helped to bring people in, bring them back into the group, continually… It was done very seamlessly, very unobtrusively, but I certainly noticed, we all as a faculty noticed who was doing it, and how they were doing it, and it was great. You don't always see that, I have to say… There were key people. They've got the momentum – and I think we know the people we're talking about there – and they were driving things forward, and again done in a very nice way, a very enthusiastic way. Because within a team you always find a degree of fragility at times… It can be depressing not getting things to work when you've got high hopes, and I think as a team they worked really well together. That's nothing to do with us; I think that's to do with the personalities and the abilities of the people in the group.

There was a very different feel to Roger's view of the Imperial College team:

> I felt frustrated by the team actually. The team didn't communicate to their advisors as much as they should have. They weren't communicating well across the team and they were a bit lethargic. And this is something we've never had before. We've always had very responsive teams – and we couldn't quite put the finger on it this year. We didn't know whether it was personalities or whether the team just didn't gel.

Certainly, this group seemed to face more challenges and communication difficulties than I witnessed at Cambridge – and yet, this was undoubtedly a very dedicated, highly intelligent and friendly group of students. Perhaps the different dynamics across these teams – at least, as judged by senior advisors – is partly also a result of different paces and degrees of successful outcomes (discussed in Chapter 5). I would also venture that different institutional cultures, values and approaches – one that has a tendency to follow creative ideas with a less competitive edge (Cambridge) and another that generally pursues applications with a highly competitive rigour (Imperial College) – influenced how the teams and ideas evolved over the course of these projects.

Adding to that point, these different institutional cultures are indicative of the currently multiple – and sometimes divergent – ways in which to understand and perform synthetic biology more generally. Speaking on the approaches to this emerging field, and again separating biologists and engineers, Roger pointed out:

> It depends on the university but I suppose that certainly at Imperial, we're more applied in our thinking… We're using synthetic biology to solve problems, so it is very much an engineering approach. That is what engineers do – they solve problems. Biologists, you know, explore and try to find out how things work – they don't necessarily solve problems. Biologists solve hypotheses not problems – hypotheses and problems, as you probably know, are slightly different. Synthetic biology is not a hypothesis driven science – it probably wouldn't be very successful if it were… At Imperial College, we've got a bunch of engineers and students who want to do

> something. I think that's the power of this field. Now, other universities don't necessarily do that – most do. Cambridge wants to develop technologies that could be useful ultimately, but perhaps they're not as hard-core applied as we are.

At Cambridge, Samuel contended:

> There are those great fans of *the engineering approach*… and, there's actually nothing wrong with that if you've got a mature technology to underpin it. If for example, you have digital electronics, you want to make some kind of device and it's simply a matter of finding the best way of assembling the underpinning logic to do that, then cool, no worries. But in biology, it's a little less tangible than that because the rate-limiting step is actually finding the function and you don't have, at this point, modular, universal tools to put things together. What you have is the biosphere and you need to pull out the various pieces that you need from the biological literature… And these are all naturally evolved systems and actually you have this huge diversity of function. It's a bit like mining…

Synthetic biology aspires to a mature technology state of having off-the-shelf components – and has gone some way with BioBricks (albeit a limited number that function reliably across different experiments) and bespoke online services to design and synthesize DNA. However, the technology remains *immature*, very flawed in practice and in need of a great deal of mining for suitable materials. Samuel added that, the Cambridge view is driven by the richness and "untapped nature" of biological resources. He continued:

> Real innovators in biology's history… didn't set out to make some kind of astounding discovery – they were curious people who were out looking to make lateral connections. And if you have a top-down approach you miss lateral connections by definition, because you've defined the project already. But if you have a degree of freedom to investigate, to think, so that the brainstorming process doesn't end with the definition of the project but rather continues with investigation of the parts – as it should, as any kind of scientific endeavour should maintain that degree of flexibility. I know to my core that that's how innovative biologists work…[111]

[111] When Samuel explained this view to me, he told stories of famous biological discoveries that were the result of serendipitous explorative-style research – for instance, the group who

These passages point out intriguing differences in approaches to synthetic biology. Recall that one aspect of the Imperial College project was certainly that once they had their modules and project overview, they stuck with that top-down design and drilled down into each module, trying to attain enough results to build a proof of concept argument for each section. The Cambridge group had an overview in which the project evolved but, as the reader will see in Chapter 5, there was a good deal of lateral thinking when, later in the summer, they were challenged by designers to really think about how their work might fit into a broader context of applications and implications. Thus far, it should be clear how different frameworks for thinking about, and doing, synthetic biology are *in-the-making* and *contested* at this field's presently early stage.

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accidentally discovered Green Fluorescent Protein (GFP), a luminescent protein found in jellyfish that has turned into one of the most revolutionary tools of contemporary bioscience.

5. MAKING REAL

This chapter describes the tangible new biological entities that the teams constructed. An overview of each group's final results is given and some missed goals as well as potential futures for E. Chromi and the E.Ncapsulator (the playfully titled final projects of the Cambridge and Imperial College teams respectively). I also revisit Hacking's (1983) position as a 'realist about entities and an anti-realist about theories', claiming that, although the projects do not fulfil their hoped for forms, there remains good reason to pay attention to the fact that undergraduates, working in a limited time frame, are capable of engineering new biological machines that operate according to bespoke design. Ideas on 'machine' and 'organism' are also highlighted, provoking consideration of how humans may interact with potential future breeds of living machines.

5.1 Making real at Cambridge

E. Chromi: final results

Impressively, the Cambridge team brought in initial tangible results as early as week three when they effectively introduced genes encoding MelA (brown pigment production), violacein (purple) and carotenoids (orange/yellow) into *E. coli* cells (Figure 5.2). However, there was a great deal more to be achieved in terms of successfully designing, operating and testing the constructs to fit the BioBrick format. Over eight more weeks were spent looping around a design and experiment cycle, doing a great deal of troubleshooting, even after the team's early success. Notably, this group's three major colour generators were made by different means, demonstrating a range of BioBricking techniques (Figure 5.1).

Figure 5.1: Colour generator achievements

Colour Generator	Achievement
MelA	MelA is mutant gene from a *Rhibozobium etli* bacterium. This gene encodes for a macromolecular compound that produces a characteristic brown colour. Lucky for the team, Douglas had a stock of plasmids that carried MelA. The team was able to extract this gene, amplify it to generate thousands of copies (using PCR, as described in Figure 4.4) and put these into *E. coli* hosts – this was all done using basic microbiology tools and protocols. The group further designed MelA by adding the appropriate features of a BioBrick (detailed in Chapter 4). Testing this construct's compatibility – proving that it 'clicks together' with other BioBricks, as the Lego™ analogy implies – was the final, and successful, step.
Violacein	With violacein (originating from *Chromobacterium violacein*), the first round of experiments was again swiftly accomplished because Douglas had a working construct that students could use. Indeed, they were able to put this construct into *E. coli* and have the cells produce purple. However, when it came to turning this genetic unit into BioBrick form, as already discussed, the group realized that synthesizing the gene from scratch with a nuanced design would achieve much more exciting results as it could be engineered to produce multiple colours.[112] The group succeeded at producing two shades of green and violet; with additional time, it was likely that this construct could yield at least one further colour, though the team could not do so before the Jamboree.
Carotenoid	Experiments on the carotenoid system (originating from *Pantoea ananatis*) began by using existing BioBricks from The Registry (constructs made by previous iGEM teams). However, upon experimenting with these BioBricks, the Cambridge team realized that there were ways in which these constructs could be improved. Senni made new carotenoid devices under enhanced regulatory control and achieved better output when he used a different strain of *E. coli*.[113] Figure 5.3 is the data sheet that Senni made to characterize the Lycopene-producing device – this thorough characterization of BioBricks that are given back to The Registry is an important goal for iGEM teams, though few groups manage to get this far.

[112] Also notable, the initial Vio operon from Douglas had "many forbidden restriction sites" and so could not be submitted to The Registry without a good deal of bespoke alteration.
[113] http://2009.igem.org/Team:Cambridge/Project/CA02; http://2009.igem.org/Team:Cambridge/Project/CA03.

Figure 5.2: Colour producing bacteria

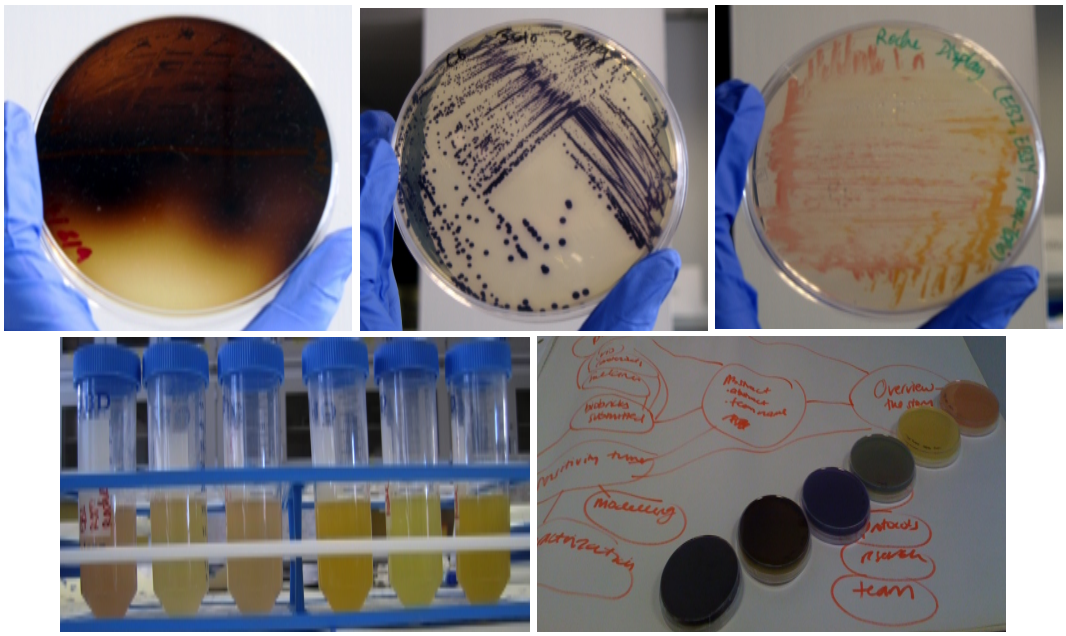
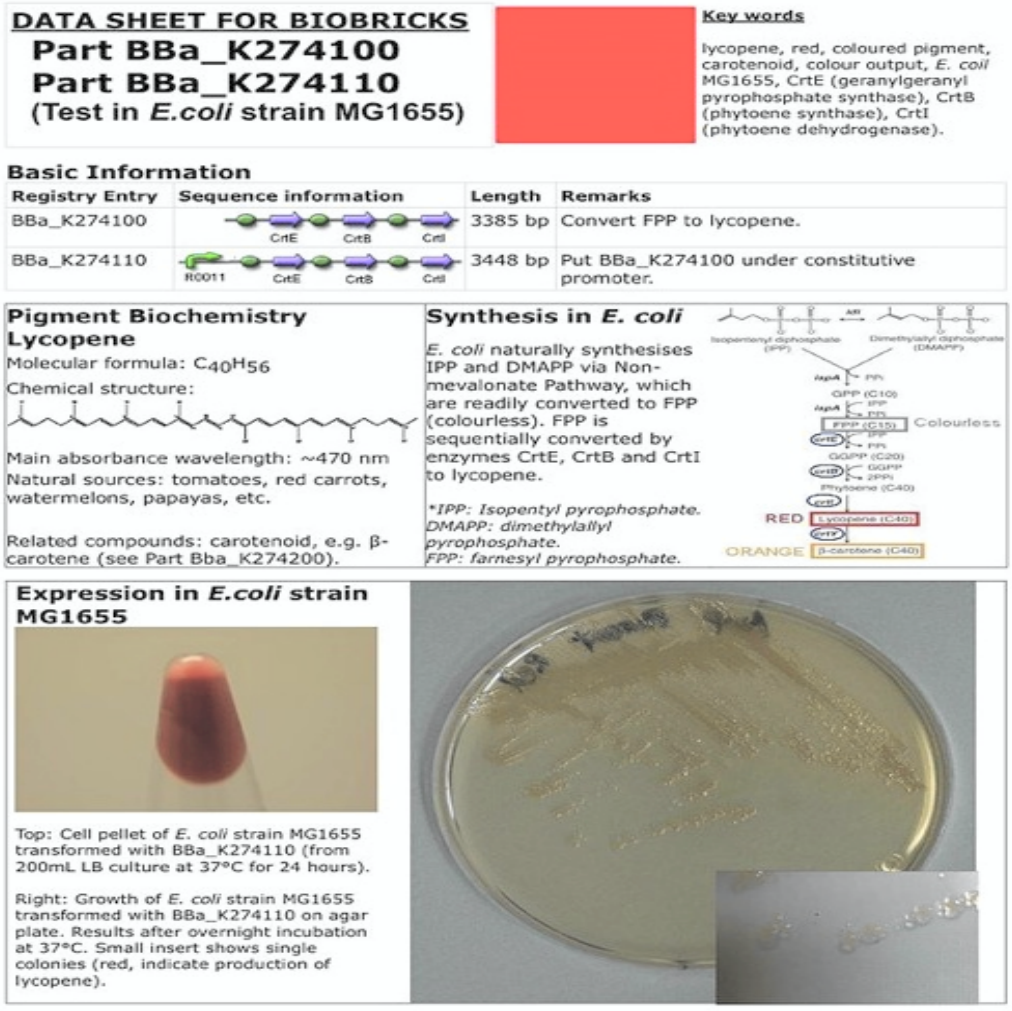


Figure 5.3: Lycopene Data Sheet



DATA SHEET FOR BIOBRICKS

Part BBa_K274100

Part BBa_K274110

(Test in *E.coli* strain MG1655)

Key words

lycopene, red, coloured pigment, carotenoid, colour output, *E. coli* MG1655, CrtE (geranylgeranyl pyrophosphate synthase), CrtB (phytoene synthase), CrtI (phytoene dehydrogenase).

Basic Information

Registry Entry	Sequence information	Length	Remarks
BBa_K274100	CrtE CrtB CrtI	3385 bp	Convert FPP to lycopene.
BBa_K274110	R0011 CrtE CrtB CrtI	3448 bp	Put BBa_K274100 under constitutive promoter.

Pigment Biochemistry

Lycopene

Molecular formula: $C_{40}H_{56}$

Chemical structure:

Main absorbance wavelength: ~470 nm

Natural sources: tomatoes, red carrots, watermelons, papayas, etc.

Related compounds: carotenoid, e.g. β-carotene (see Part Bba_K274200).

Synthesis in *E. coli*

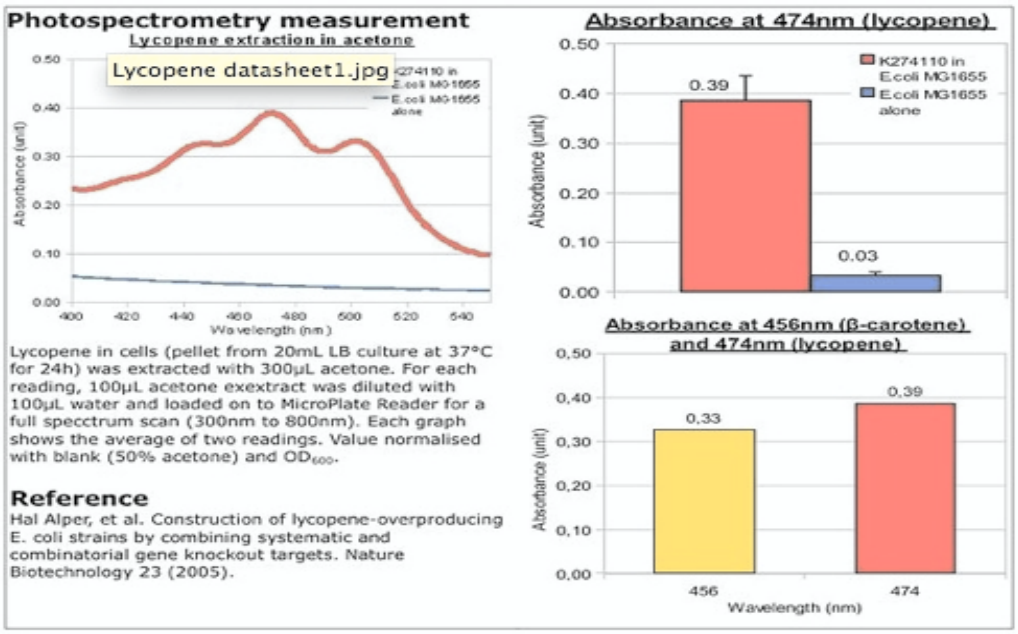
E. coli naturally synthesises IPP and DMAPP via Non-mevalonate Pathway, which are readily converted to FPP (colourless). FPP is sequentially converted by enzymes CrtE, CrtB and CrtI to lycopene.

**IPP: Isopentyl pyrophosphate.*
DMAPP: dimethylallyl pyrophosphate.
FPP: farnesyl pyrophosphate.

Expression in *E.coli* strain MG1655

Top: Cell pellet of *E. coli* strain MG1655 transformed with BBa_K274110 (from 200mL LB culture at 37°C for 24 hours).

Right: Growth of *E. coli* strain MG1655 transformed with BBa_K274110 on agar plate. Results after overnight incubation at 37°C. Small insert shows single colonies (red, indicate production of lycopene).



Sourced from: http://2009.igem.org/Team:Cambridge/Project/CA05.

In addition to the success of the colour generators, the Cambridge 2009 team built on the work of their 2007 predecessors and constructed a series of sensitivity tuners. The detail of this section of the project is too technical for non-specialists so I refer those interested to the team's Wiki.[114] In essence, this section of the project addressed how some biosensor devices necessitate extreme sensitivity to a given input (e.g. to low concentrations of a toxin in water or the atmosphere) while also having an appropriate output indicator (e.g. a strong and sustained signal). The team therefore made a collection of tuner devices with a range of sensitivity levels that could be parts of future biosensors. Also notable, the team focused on good characterization of their tuner BioBricks, demonstrating an incremental step forward in building on previous synthetic biology work. Interestingly, there is something at odds in terms of how the iGEM competition tries to promote development of the field: on the one hand, blue sky ideas are

[114] http://2009.igem.org/Team:Cambridge/Project/Amplification; http://2009.igem.org/Team:Cambridge/Project/Amplification/Characterisation.

encouraged and celebrated as inspiring for students, but such projects mostly cannot be realized in functioning new synthetic biological systems; on the other hand, it is perhaps a more productive approach to make smaller, incremental improvements on existing work as this is far more likely to yield reliable, usable material forms. With flashy colours and a clever set of improved sensitivity tuners, this team captured the best of both kinds of desirable iGEM results.

Before moving on to describe how the team envisioned the future implications of their project, the following two figures show other representations of real results. In Figure 5.4, note that "things built" were still identified in cartoonish illustrations, posted up around the lab, checking off accomplishments as the team neared the competition. Figure 5.5 illustrates different forms of modelling. The first part shows ordinary differential equations that were used to mathematically trace rates of reaction (e.g. the rate at which genetic material is transcribed in experiment), concentrations of reactants or the relative activity of a promoter[115]. Note too that the team included a written explanation of their mathematics. Experimental data was entered into various differential equations, sometimes run through simulation software and graphed. Graphs enabled better description of what was going on in a given part of the biological system and sometimes helped in forming predictive hypotheses.

[115] See Key terms, p. 11.

Figure 5.4: "Things Built"

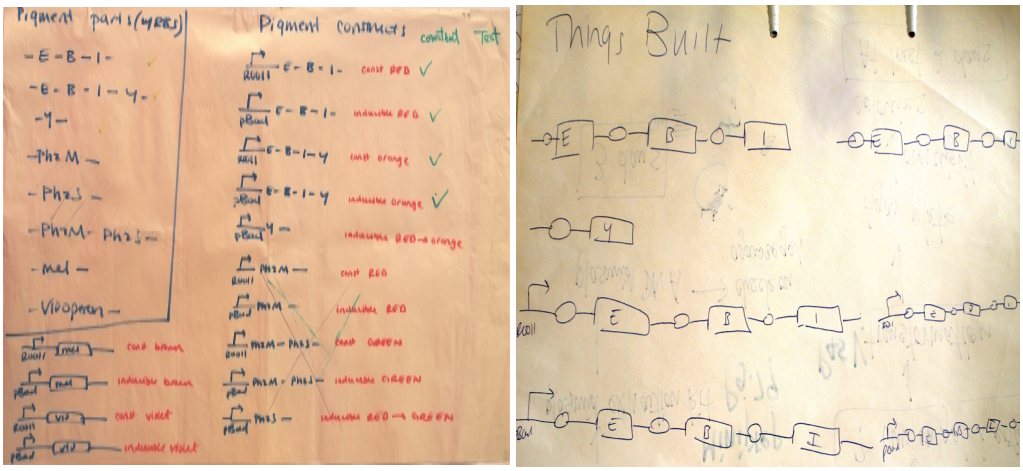


Figure 5.5: Basic modelling mathematics; example graph; example data analysis

Modelling the phage activator system

This is the basic 'amplifier' system that consists of an input sensitive promoter system,a protein activator and sensitive promoter. It can therefore be divided into two boxes, the approach taken in putting forward an initial model.

The pBAD promoter

An arabinose input acts as an inducer, permitting transcription, by binding the AraC transcription factor. This is a dual transcription factor; when unbound to arabinose a dimer restricts access of polymersase to reduce basal levels of transcription, upon binding arabinose the conformation changes and the dimer permits binding of polymerase. [1]

To model this situation, araC is first assumed to take the role of a repressor that reversibly binds and unbinds a site on the DNA. If it binds arabinose, it is sequestered and cannot bind the DNA. Here, an input function is created, after Alon [2]. This gives the rate of transcription from the promoter dependent on the concentration of arabinose. Since mRNA is then translated at a roughly constant rate, it is related with a multiplicative constant to the rate of protein production, in this case activator and RFP.

$$F_{input}(X^*) = \frac{\beta_{max}}{1 + \left(\frac{X^*}{K_d}\right)^n}$$

This gives the rate of transcription as a function of X* which represents the concentration of active repressor, unbound to arabinose. B is the maximum rate of transcription, here this rate is when induced by arabinose at highest concentration. K_d is the dissociation constant (see modelling derivations). Parameters must be found by a parameter scan for sensible values or by comparing to already gathered data.

The concentration of 'active' repressor is given as a function of arabinose concentration by:

$$X^* = \frac{X^T}{1 + A^n/K^n}$$

where X^T is the total amount of araC available, bound or unbound. A is arabinose concentration. n is the number of arabinose molecules binding to each molecule of the repressor, and K is a binding constant. n was taken to be two by assuming that each araC dimer needs two molecules to be bound before it can permit transcription.

Combining these two gives the overall input function, which has leaky transcription included at A = 0, seen in the actual results.

The Activator and its Promoter

This is based on a similar idea. Activator is made by transcription from pBAD, the mRNA is then translated (the potential time delays will be taken into account). The activity of the phage promoter is dependent on activator concentration according to:

$$promoter\ activity = \frac{\beta X^n}{X^n + K_a^n}$$

Assuming that translation rates remain constant, the rate of GFP and RFP production would be expected to be multiples of the above promoter activities/ input functions (which represent rate of transcription)

The aim of this area of work is to fit the activator plate reader to curves in an attempt to better charactertise them in terms of hill function parameters after Canton [3].

Entire System

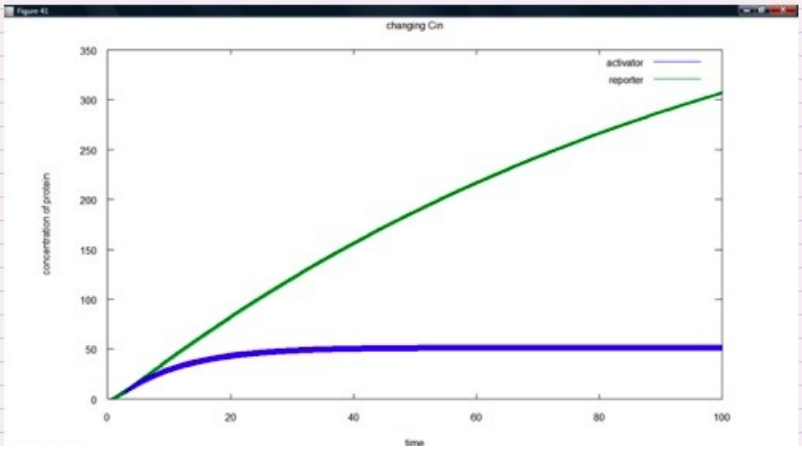
The entire system, although a collected of nested hill functions, has an overall sigmoidal response to input concentration. This means that the full system can be modelled as a hill function, with appropriate parameters obtained by experimental analysis.

Modelling

We have now developed several versions of our model for the amplifier. These involve a simple model, positive feedback and degradation of the activator protein. We also included dependence on a parameter for input transcription, describing changes in both arabinose concentration and binding properties.

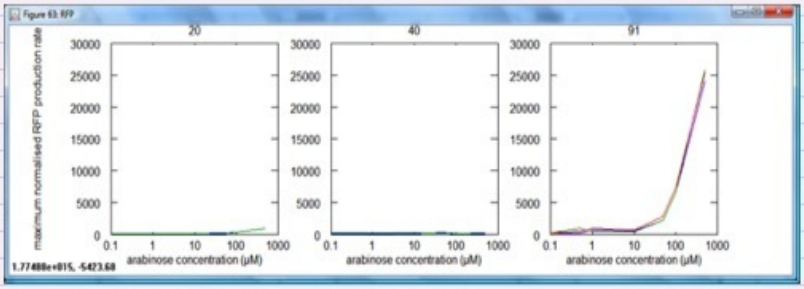
We have some interesting results for the positive feedback latch. Our *continuous* model indicates that whatever the transcriptional input, the reporter is produced in the same way. This means that the latch would be switched at any input level. We plan to look at stochastic modelling to see if the same applies here.

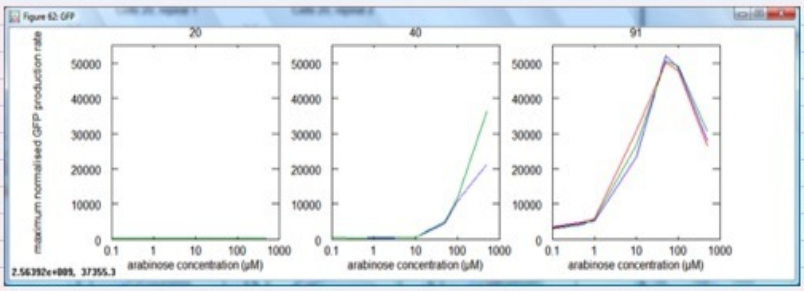
We produced several graphs to show what happens when different parameters are changed for the latch. The most important is the following, showing the very small effect of changing transcriptional input - encapsulating the effect of different arabinose concentrations.



Data Analysis

- For each data set, the maximum normalised fluorescence rate was taken. This is the measurement used to calculate Relative Promoter Units, and by extention, RNA Polymerase per second (PoPS). These data were plotted for each cell type against concentration of arabinose:





The most important graphs above are those for GFP in cells 40 (pBAD) and 91 (amplifier). These are effectively the input and output for the amplifier device. One can see that the pBAD curve has no real increase until at least 10μM, whereas an equivalent large increase for the amplifier starts at about 1μM. Very low level transcription can be seen to be amplified. The amplified graph (91) starts to drop off at high concentrations: this may be due to toxicity.

Sourced from: http://2009.igem.org/Team:Cambridge/Modelling; http://2009.igem.org/Team:Cambridge/Notebook/Week5.

Potential futures

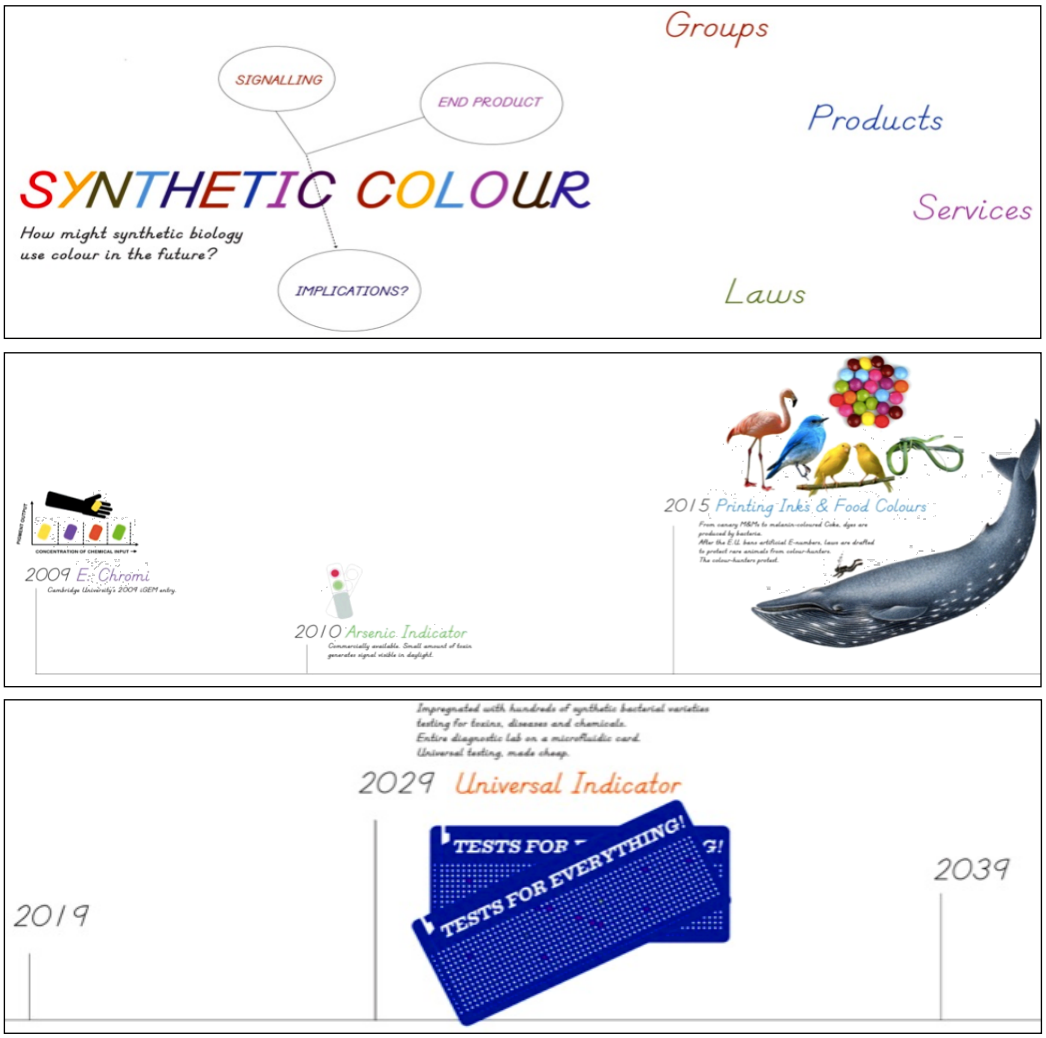
Mid-way into the summer work was really under way, and students had a tendency to focus on ticking off the long list of important experimental and modelling tasks at hand. Sometimes the wider implications were lost sight of. Luckily, the revisiting of interaction designers[116] Daisy Ginsberg and James King[117] was well timed – the team had a good idea of their project's goals, but they had not yet begun thinking about presenting and contextualizing their work. Daisy and James had taken the synthetic biology crash course (Chapter 3) earlier that summer to begin informing their design work; however, they remained intrigued about where the iGEMers' project was leading and agreed to return to Cambridge to run a design workshop for the students to help them think about their project's future implications. This workshop was also the start of what was eventually a highly celebrated design project that Daisy and James created and presented, not only at the Jamboree, but also in several other shows around the world.

Knowing that the team was working on a pigment-producing *E. coli*, Daisy and James began their workshop by proposing seven hypothetical scenarios, from the present to one hundred years into the future, that focused on groups, services, laws and products that might be oriented around this project idea. Through illustrative storytelling (Figure 5.6), these designers led students, advisors and myself through an imagined future in which engineered colourful bacteria allowed the production of an easy-to-use, colour indicator arsenic biosensor (ambitiously proposed for 2010); later, a world in which "colour-hunters" unlawfully scavenge the living

[116] See Key terms, p. 11.
[117] http://www.daisyginsberg.com/; http://www.james-king.net/.

world in search of colours for printing inks and food dyes (2015); then, a world in which hypochondriacs could have their very own "scatalog" by consuming a colour-producing, bacteria-infused yogurt drink that would be specially designed to reveal one's state of health through colourful faeces that could be mapped according to a disease chart (2049); finally, in 2099, the proposal entailed a world in which colour is everywhere, acting as a permanent reporter of ambient mood sensing, with surfaces in homes and on everyday materials being composed of living, colour-generating machines.[118]

Figure 5.6: Synthetic colour design futures workshop

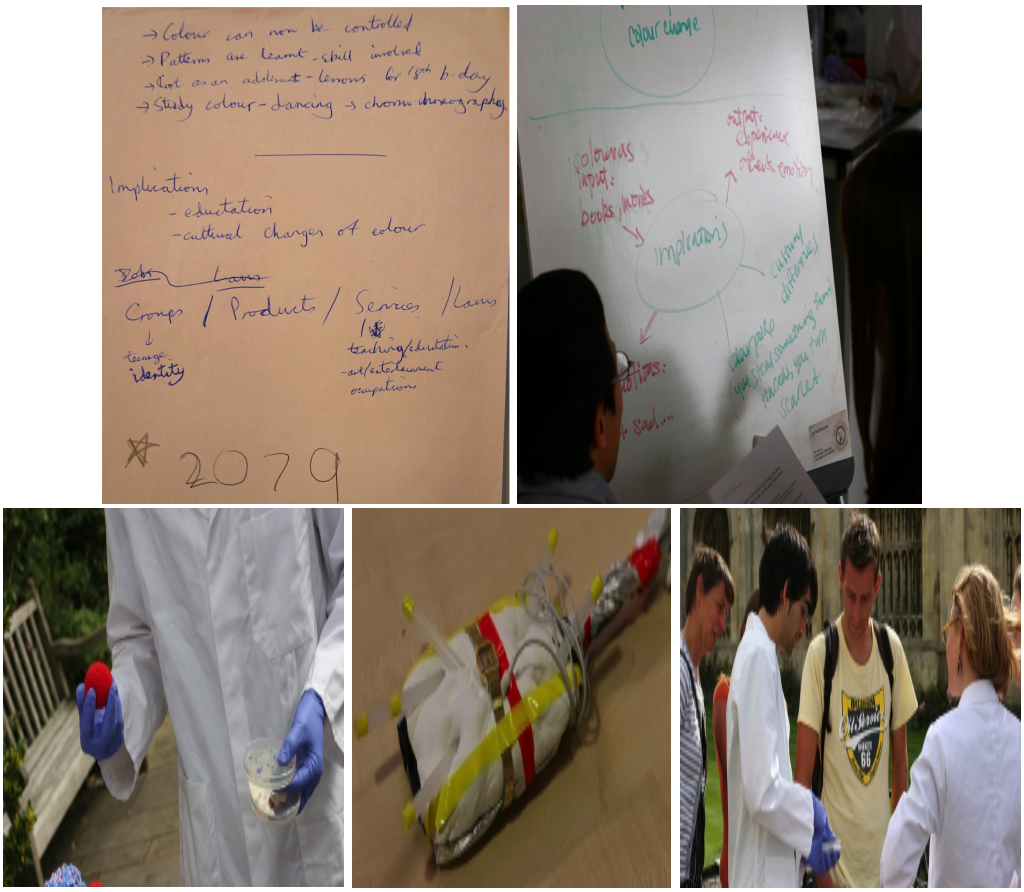


[118] http://www.echromi.com/.

…

Such elaborate scenarios provoked the group to reflect upon both positive and negative possible future implications of synthetic biology, and we (students, advisors and myself) were then split into groups of three or four and asked to come up with our own provocative stories to fill in the timeline. Armed with a suitcase of props (with everything from face paint to rubber balls, pipe cleaners and Petri dishes), we were encouraged to spend a couple hours thinking creatively, talking to strangers in the street, getting into character, crafting a skit – in short, to go wherever our imaginations could take us. It was quite amazing when the team reconvened to present and discuss what was learned in stepping away from the molecular-scale work, turning to an exploration of macro-scale social, cultural and ethical implications projected into a possible futures realm.

Figure 5.7: Brainstorming potential futures



The team returned to the workshop room with renewed energy and excitement (which had been slightly deflated through weeks of monotonous laboratory work), thrilled to tell the rest of the group what they had imagined for a future world dominated by colour-producing synthetic organisms. One group explored how synthetic biology might be used in a range of products – from children's toys to food dyes – and they went out into the streets of Cambridge, asking members of the public about their feelings on such products. They posed questions such as:

- 'In the future, would you want to buy your children a genetic engineering kit that allowed them to build their own microorganism – something they could dress up with fancy colours and designs, while

learning about science?' (Responses to this question were generally positive, though so was the framing.)

- 'How would you feel about consuming food that had been genetically engineered to incorporate colourings from the living kingdom? For instance, would you find it suitable (or even more appetizing) to eat vegetables that were flamingo pink?' (People tended to think this was a bit absurd and were generally not keen on this idea. Still, some agreed that this seemed possible and even commented that they could see it as a future trend of haute cuisine.)

A debate was brought up about whether or not it would be right for colour-coding genes to be patented. One group took this issue to extreme in a skit where they envisioned a world in which the colour orange was patented and under strict control – much to the anger of a popular mobile phone provider as well as countries whose national flags were meant to contain orange. This skit led to the enactment of a scene in which a rebellious group – "the orange liberation front" – sought to terrorize the orange patent-holders (see the bomb prop that students constructed in Figure 5.7). Another group discussed the role of "colour hunters" in a world in which several industries were trying to produce new trends in colourful products and services. Almost every story that was dreamed up during that workshop seemed to be an outlandish and unlikely future scenario; yet, this exercise effectively prompted students to think about their work's potential future applications and ramifications – good and bad.

The team eventually scaled back the creative design exercise and settled that, for the competition, they would present the realistic near(-ish) future of their work that

it might provide an improved, easy-to-read colour output for an existing biosensor (specifically, the arsenic biosensor device that the 2006 Edinburgh iGEM team had constructed[119]). Though the Cambridge team did not do an expanded human practices project[120], in light of these design workshops, students were clearly inspired with a greater awareness of how synthetic biology might generate future tools, products and abilities that could change how we see ourselves in relation to the biological world. Furthermore, it was through a *creative engagement* – and one that was somewhat in line with the imaginative brainstorming that started the students' iGEM process – that genuine curiosity in human practices subjects was sparked across the team. I felt fortunate to be involved in these interactive workshops as a participant, rather than talking to the students in a quasi-instructor way about how to develop a human practices side project. Furthermore, I noticed that after the design workshop, more students asked about my research and several additional conversations about social and philosophical implications of synthetic biology were had as time moved closer to the Jamboree.

It was ideal to mix my everyday, casual conversation, along with the imaginative design workshops that inspired bigger picture thinking among this team over the course of the summer. Geoffrey commented on the effectiveness of an unconventional approach:

> People should be taking more on board that traditional ways of learning, if you want to call it that, probably don't work in these kinds of contexts. You can go and give a lecture on all of these bigger implications things and you can have somebody listen to ethics, but

[119] Edinburgh 2006 project: http://parts.mit.edu/wiki/index.php/University_of_Edinburgh_2006. Note too that despite whispers of collaboration, the connection of *E. Chromi* to the Edinburgh biosensor has yet to be realized.

[120] I did offer to help the students with a human practices project, but given that they had the designer input and plenty to do, they decided to simply write a brief synopsis of their thoughts from the design workshop: http://2009.igem.org/Team:Cambridge/Future.

> basically the kids are just going to… yawn, OK, and they won't learn anything. But when you talk about it in the context of what they're doing and you're asking – it's insidious in a certain way – but actually that's the best way to learn. And the best way to understand how the process works is by participating in it, not being lectured at.

He went on to rave about how iGEM is particularly important to the advisors as a unique, enjoyable teaching opportunity that fully embraces lateral thinking and interdisciplinarity – that is why they make this summer experience not only include science and engineering, but also business minds, designers and social scientists. Geoffrey said of doing iGEM properly, "you can't do it without engaging all of it… all of it in parallel and seriously". In later chapters, I continue to highlight the influence of design interactions on the Cambridge team and in synthetic biology more broadly.

Before moving on, it is important to recall one other matter on the potential futures of iGEM projects: because teams give their created BioBricks back to The Registry, the colours and tuners that the Cambridge team made will undoubtedly live on in a number of future iGEM incarnations, yet to be imagined. Of course, the same applies for all useful BioBricks made in iGEM.

5.2 Making real at Imperial College

The E.Ncapsulator: final results

As a versatile drug-manufacturing platform for targeted delivery of therapeutics to the intestine, The E.Ncapsulator set its project aims very high; it was not surprising that the Imperial College team achieved a fraction (about 30%, according to Olivia) of their overall vision. Additionally, the most impressive and substantial results were obtained almost at the last minute, as the team worked

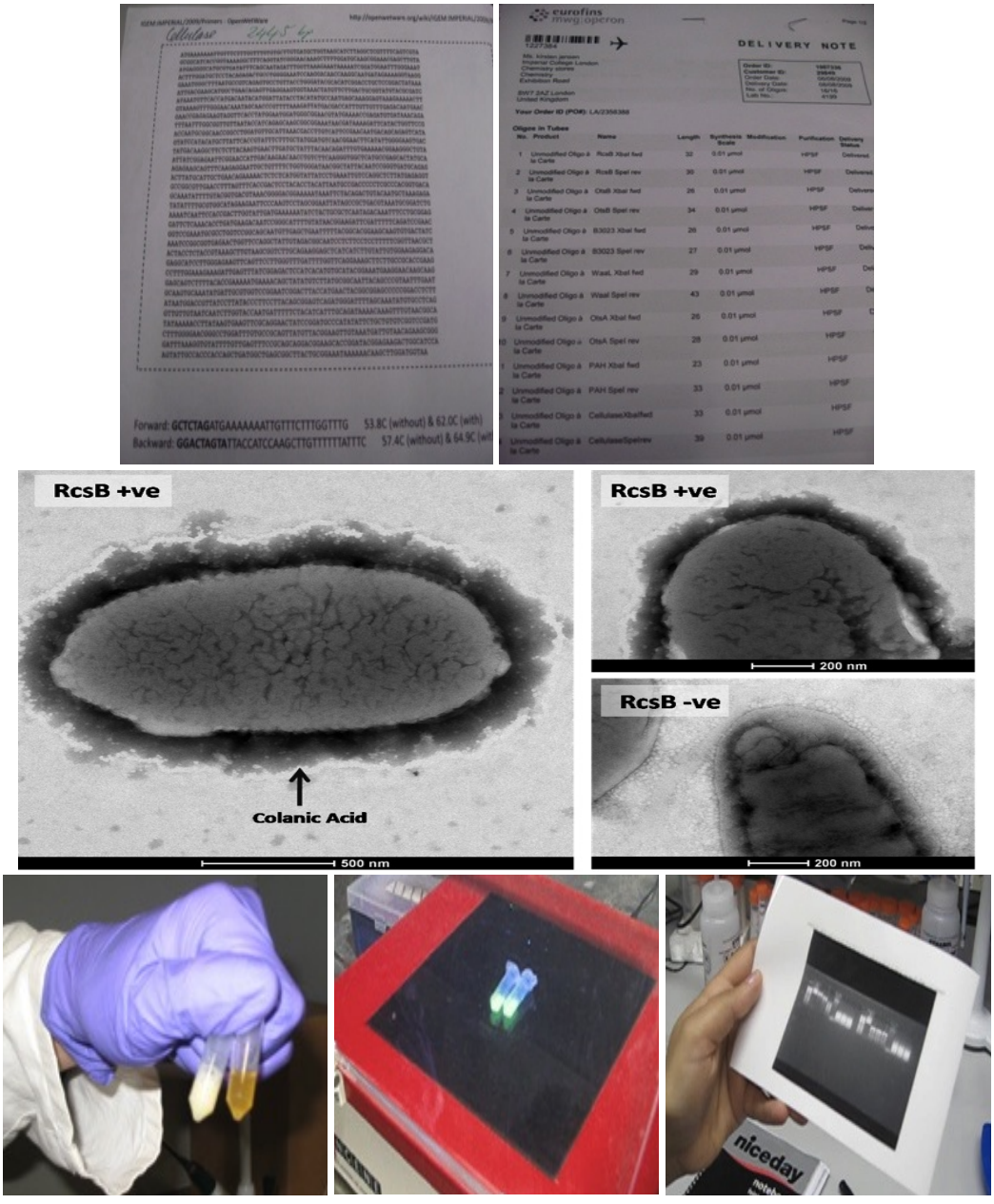
tirelessly in the wet laboratory right up to the day before departing for Boston. Recalling the heavily structured and modular project that was outlined in the last chapter, notably, the team developed a strategy that progressively filled in as much data (real and hypothetical) into each section as their design and experiment work progressed. Still, a good number of results (or, at least proofs of concept) were achieved and described on the team's Wiki and in their presentation at the Jamboree. The next chapter explores how this team was coached in expertly selling their project but, for now, I shall describe what was actually made real.

In module one (protein production), the team was unable to construct cellulose. This section was intended to be simple as students ordered the necessary DNA from a synthesis company and would only have to effectively put this construct into cells; however, it was hypothesized that the fatal flaw came in the form of a typo in their order (all it would take is an error in the typing of a sequence of ATCG nucleotides that they ordered from a DNA synthesis). Figure 5.8 (top row) includes a photo of the cellulase sequence as well a receipt sent back to the team for their ordered synthetic DNA – which was non-functional. Still, the team did produce the PAH enzyme, allowing them to tick a box in module one.

In the next step of the project, the team showed their auto-induction switch from module one to module two (whereby a change in the bacteria from consuming a primary metabolite to a secondary one triggers another genetic change) could work; this achievement also generated nice data for the modellers. The whole team agreed enthusiastically that their biggest achievement was to get *E. coli* to secrete and coat itself in colanic acid; for this, they had visual evidence (see the

EM photograph in Figure 5.8 and note how the RcsB+ result shows an encapsulated *E. coli* and the RcsB- control shows a bacterium that was naked of the colanic acid shell).

Figure 5.8: Making some of the E.Ncapsulator real



The thermoinduction switch to module three was minimally successful in reality, though to gain some data there, the team used the ever-popular ‘proof’ of genetic

activity by showing different degrees of fluorescence in their construct at different temperatures (Figure 5.8, bottom row).[121] Module three – genome deletion – did not work in *E. coli*. The team was able to show *in vitro* (in a test tube) that DNA was chewed up by restriction enzymes but they could not show this working in a living organism. Stretching this result, the group tried to sell this *in vitro* result as a proof of concept though not being able to operate *in vivo* essentially meant that this aspect of the project failed. Another visual appeal – showing the result of a restriction digest in an agarose gel electrophoresis experiment – was used (the last photo of Figure 5.8 illustrates how DNA has been chewed up into different fragments, the relative length of which can be seen according to the positions of bands on the resulting photograph).[122]

As the competition's climax moved nearer and it became clear that some aspects of the project wouldn't work, the team continued to design experiments that would further prove – or at least *sell* – their project vision. A series of testing experiments were designed, most of which were unsuccessful. An example of one which worked partially was that the team made a test for acid resistance of their coated bacterium – in doing so, they proved some degree of higher resistance to acid (than a non-coated bacterium), helping support their hypothesis that coated bacteria would be resistant to degradation in the stomach and so could travel to the gut to deliver medication.

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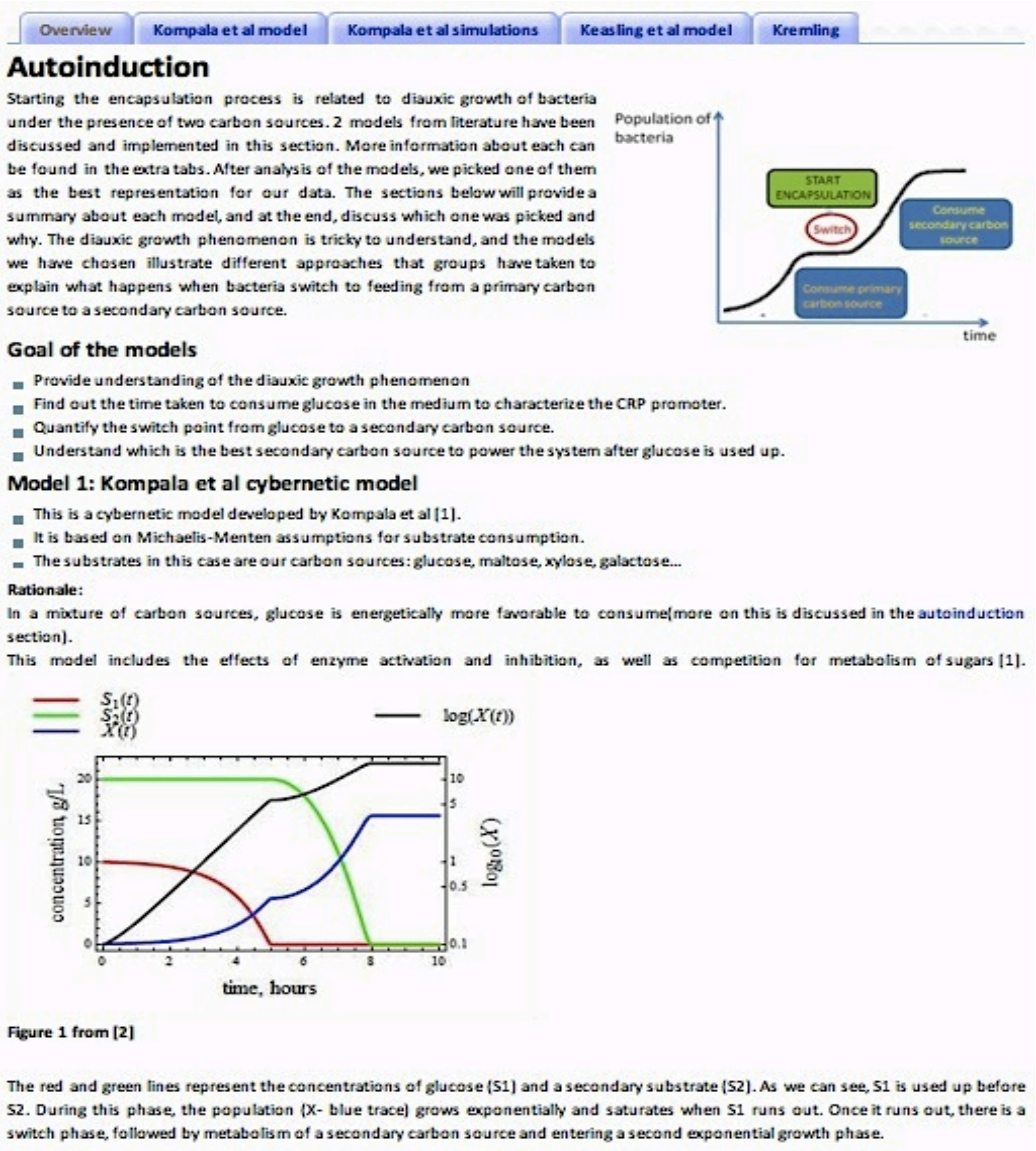
[121] Green fluorescence protein (GFP) is a common reporter gene used in microbiology experiments. When GFP is coupled to the functioning of another gene, it is used as a visual demonstration of the system working. However, as one advisor noted, "saying that something glows green doesn't necessarily mean it works!" For further on GFP, see: http://en.wikipedia.org/wiki/Green_fluorescent_protein.

[122] For further technical information, see: http://en.wikipedia.org/wiki/Restriction_digest; http://en.wikipedia.org/wiki/Agarose_gel_electrophoresis.

The modelling of autoinduction is illustrated in Figure 5.9 and though I will not examine the technical detail, I note the amount of work that was put into this part of the project. Such attention is unsurprising as, in the next section, I explain how much of the modelling was hypothetical, owing to late or failed experimental results.

Figure 5.9: Modelling example: autoinduction



Model analysis

Assumptions

- Michaelis Menten Assumptions (see drug kinetics model) have been applied in the kinetics of consumption of enzyme and substrate
- Effects of competition and induction can be represented by probabilistic variables (u and v) and are directly dependent on the rate of consumption of any given substrate Si within the mixture
- More details about assumptions made for each individual variable are described in the paper.

Predictions

- In a mixture of substrates, glucose is always used up first by the culture, and then any other secondary source present in the medium.
- The time length of the primary and secondary exponential phases of growth in the biomass depend on the initial concentration of carbon sources.
- This will help to predict the switching point between two sources.
- In our project:
  - The primary Carbon source: Provides repression of the CRP promoter and delays the start of the encapsulation phase (Module 2)
  - The secondary Carbon Source: Will power the system once the primary source has been used up. Finding the best secondary carbon source can help us draw a relationship with the output yield of colanic acid.

Learn More about the model.

Simulations

- The simulations show how the population of substrate is consumed over time for different initial concentrations of glucose and lactose.
- We also vary enzyme concentration.

Learn More about the simulations.

Conclusions

- The lower the initial amounts of glucose present in the medium, the longer it takes to get used up.

The actual model...

When a mixture of substrates is placed in a Biomass (B), the interaction of the Biomass with any given substrate (S_{i}) is given by:

$$B + S_i \; --E_i \rightarrow (1 + Y_i)B$$

E_i is the enzyme catalyzing the metabolism of S_{i }and Y_{i } is a yield coefficient for the particular substrate. They then define a generic formula for the system of differential equations given by:

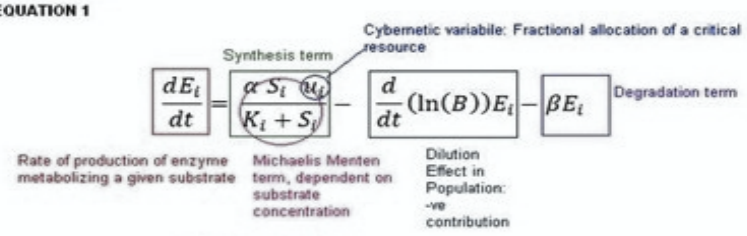
$$\frac{dE_i}{dt} = \frac{\alpha\, S_i \;\; u_i}{K_i + S_i} - \;\; \frac{d}{dt}(\ln(B))E_i - \beta E_i$$

$$\frac{dS_i}{dt} = -\frac{1}{Y_i} r_i v_i$$

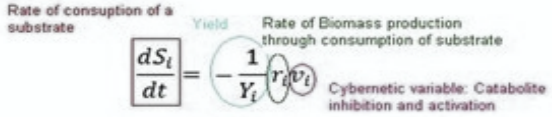
$$\frac{dB_i}{dt} = \sum_i r_i v_i$$

Further explanation:

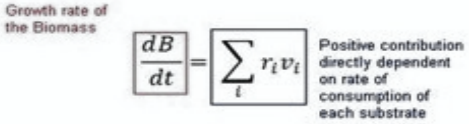
EQUATION 1



EQUATION 2

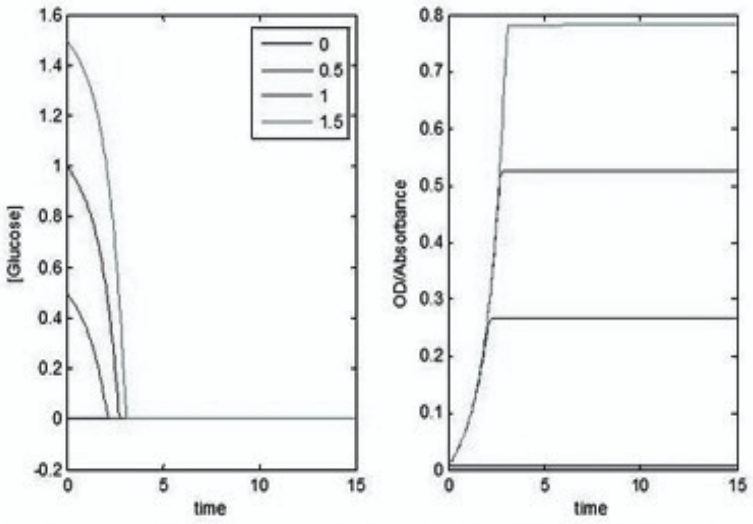


EQUATION 3



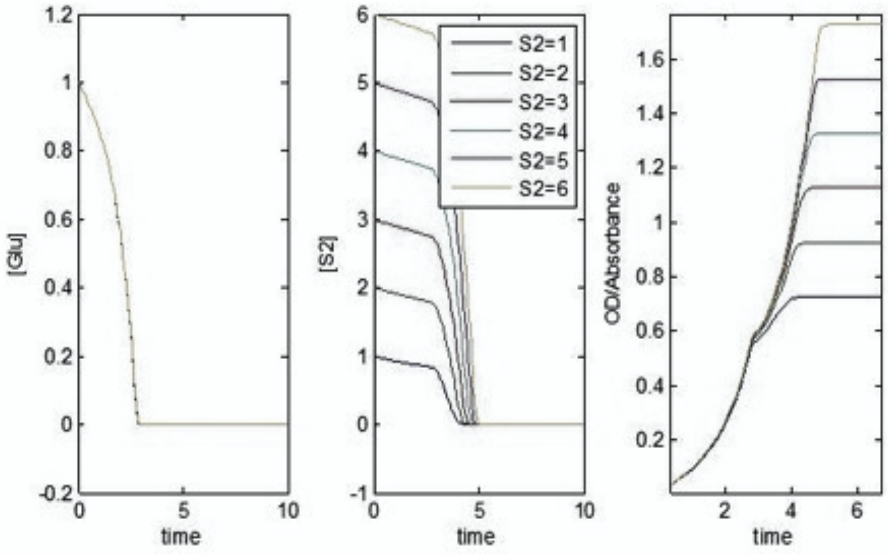
Kompala et al simulations:

1. Variation in initial concentration of glucose in the medium with a very small concentration of secondary carbon source



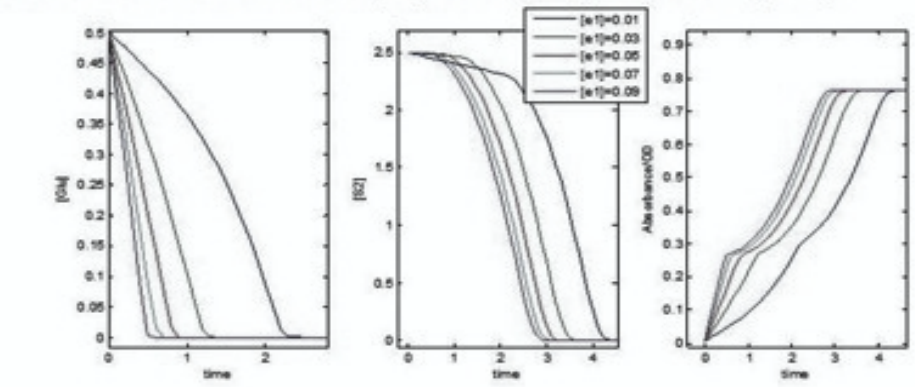
The larger the amount of glucose present immediately in the medium, the longer it takes for it to be used up and the population grows more before it reaches a point of saturation. This is an example of resource limited growth. It is not diauxic growth because there is a low concentration of secondary source, so it is not sufficient to start a second exponential growth phase in the bacterial population.

2. Fix the initial concentration of glucose in the medium and sweep through different initial concentrations of secondary carbon sources



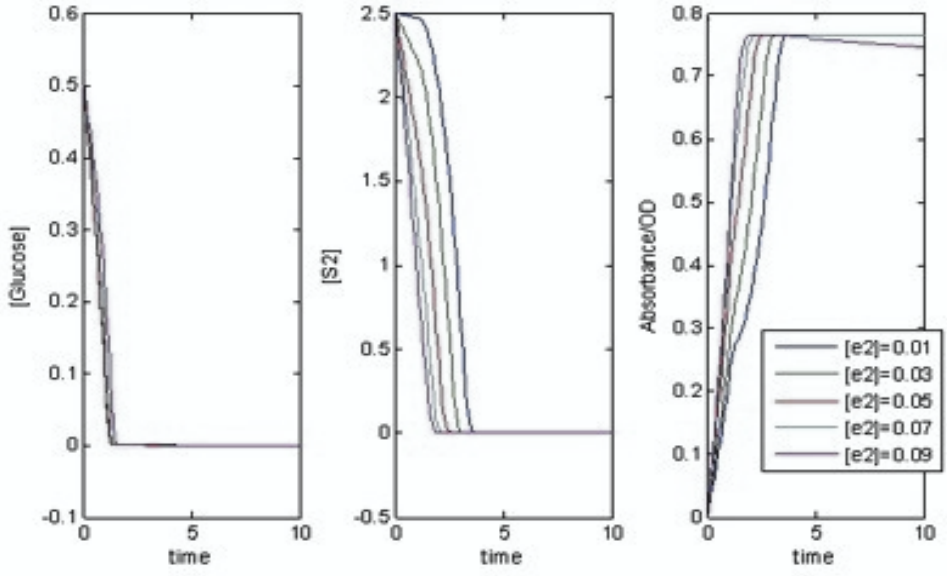
Now, we fixed the primary source [Glu]= 1 and varied [S2] (Secondary source) from 1 to 6. The lower the amount of S2, the shorter the second exponential phase and faster saturation of cell growth.

3. Variation of initial concentration of e1 (enzyme metabolizing primary source S1-glucose)



As expected, a higher e1 concentration initially, means faster consumption of glucose so we hit the 2nd exponential phase quicker than with a low concentration of the enzyme. Furthermore, if there is less e1 initially, it takes longer to consume S2 by consequence, so we can see longer delays in reaching the lag phase, and consequently, the second exponential phase.

3. Variation of initial concentration of e2 (enzyme metabolizing secondary source S2)



The less e2 present, the longer the lag phase and the slower the second exponential growth phase. However, as amounts of e2 are increased, the lag phase is not visible and the transition between primary and secondary growth is faster. In theory, e2 should only affect the secondary exponential phase. In practice, enzymes compete and the amouns of e2 also affect the metabolism of the primary source, hence why the glucose metabolism is changed too.

Sourced from Imperial College Wiki, Autoinduction sections:
http://2009.igem.org/Team:Imperial_College_London/Drylab/Autoinduction;
http://2009.igem.org/Team:Imperial_College_London/Drylab/Autoinduction/Model1;
http://2009.igem.org/Wiki/Team:Imperial_College_London/Drylab/Autoinduction/Analysis/Kompala;
http://2009.igem.org/Team:Imperial_College_London/Drylab/Autoinduction/Simulations.

Finally, I'd like to detail what was achieved in the human practices section in which students participated in the workshop and interviews that I led. Despite little help from other team members (who were under pressure to 'get the real

work done'), Andrew and I synthesized the human practices exercise into two written documents (as well as an additional brochure that was brought to the Jamboree) and a brief video of selected interview clips.[123] I'll highlight a few segments from the documents and interviews to give the reader an idea of this section's output.[124]

In Andrew's summary document, the introduction attempted to justify the importance of iGEMers looking into human practices:

> As young iGEMers, a good number of us are likely to comprise the next generation of practicing synthetic biologists. It is therefore crucial that we enlarge our view to include an appreciation of this field's potential societal impacts. That is why we believe that iGEM students should think carefully about how we can help to develop this area of biotechnology in a safe and productive way, acknowledging and participating in discussions that address wider socio-political and ethical concerns. Such dialogue is already taking place at multiple levels – a number of scientists and engineers practicing synthetic biology are participating in debate and discussion with public spheres, policy makers and social scientists in order to support development that aims at maximizing benefits and minimizing potential negative impacts of the field.

The document continued to describe the workshop, group discussion and interviews that made up the team's human practices exercise. Divided into three chapters of video clips, Figure 5.10 details some interesting interview quotes.

[123] The video can be seen at: http://2009.igem.org/Team:Imperial_College_London/Ethics. Links to the two documents are on this site as well. However, as the documents were uploaded last minute (the midnight EST deadline for all teams' Wiki lock-downs, which was in the middle of the night GMT), I did not have time to check them online. As a result, there is glitch with the links to the documents online that cannot be changed – perhaps another reflection of how human practices was not really paid attention by the group who were much more occupied with uploading every last bit of 'real data' that they could as the Wiki closure deadline approached.

[124] Appendix III has copies of the two documents; the brochure is not included as it reveals students' identity.

Figure 5.10: Interview highlights from Imperial College iGEM team human practices

1: Explain your syn bio! *In this section, students reflected on the importance of making science accessible to lay audiences. Students were challenged to explain their project in simple terms, in less than one minute.*	**2: What are you engineering?** *In this section, students talked about the materials of synthetic biology, reflecting on what it means to redesign elements of life. Is there something special about this kind of work? Is this stuff like other engineering materials?*	**3: How risky?** *In this section, students talked about their efforts to address and minimize risks in their project. They also discussed their views on risks and fears circulating around this field generally.*
"The problem we are trying to overcome is to bypass the stomach and to release this protein of interest into the small intestine. So, we hope to accomplish this by getting the bacteria to produce the compound of interest, then encapsulate itself with a polysaccharide sort of coating – which is basically like a slime layer. And, once it has encapsulated itself with this coating, it destroys its genetic material – it kills itself really. This means it is no longer a viable cell. Then, you swallow the cell and, the slime capsule – we hope – will be sufficient to allow the bacteria to bypass the stomach." (Matt) "What we are doing is coming up with a new idea for a biofabrication platform. So, we are using synthetic biology and the bacterial machinery to produce drugs. The whole point of the design in our project is that we want to make a generic platform for drug production and delivery. The main emphasis is to actually be able to get these drugs through the stomach, but also to be able to have the freedom to choose what you want to manufacture." (Nisha)	**"**I think there is huge potential – it is only sort of bounded by your imagination. So there is a huge level of creativity that you are able to experiment with. Everyone has creative urges, right? But, I mean, I am no good at art, I cannot paint, I cannot draw. And this [in synthetic biology] is something where I feel you always can have some human nature artistic input, a kind of creative force – it is really cool… In synthetic biology, we have available more colours than maybe a traditional artist's pallet anyway. When you try to say to someone, 'try to picture a new colour in your mind' – and, of course, you cannot do it because your reference point is what you know already. But, you are not bounded by that in synthetic biology because so many genes have yet to be discovered. And, with every gene that is discovered, there is functionality that maybe you can employ in some kind of a nifty way." (Zach) "I'm just amazed by the idea that you've got a tiny tube and you're working with tiny volumes and you've got this clear liquid in your epindorf tube and in there is DNA – and that DNA is all assembling into something that you've designed! I think that is quite amazing – it is awesome… You don't always think about the bigger picture – it is a difficult one. I mean I try to consider the implications of what I'm doing when I'm in the lab and the effect that it will have in the bigger picture, but you do kind of	"So I can understand that it is a weird idea that you kind of pop these pills of bacteria into your body but at the same time, I think it is about getting past a certain kind of notion: getting past the fear of it and getting used to the idea. I think that will come as there are more safety tests and things like that so people are assured, 'OK, this is a safe thing to do'…" (Kajan) "I believe the technology has the potential to disseminate so fast and sort of untraceably in terms of DIY communities. So, I don't think it is as much about being able to control *activity*. But possibly being able to understand it and grow a community that is able to think responsibly. So, I guess it is a bottom-up approach to risk and that's what needs to be fostered in the nascent field." (Zach) "Scientists need to explain what the real risks are – not dim them down. The scientists need to be able to understand the fears… And sometimes fears are irrational – it is a completely different level and so they have to understand their science but also be human beings, and understand

	take it for granted that, OK, what I'm doing here is working with DNA, manipulating it and changing it – I'm changing the existing systems and how they are naturally." (Felicity)	why people fear. Whether they're right or not – that's a very valid question, whether they're *right* to be in fear or not. The dialogue is very key to the field." (Andrew)

Andrew ended the summary document with a few short paragraphs on what was learned during this session as well as some suggestions for future iGEM teams. He talked about how the team found it interesting and stimulating to be pushed in interview to articulate views on broader socio-ethical issues when often students forget to think about such matters, feeling too bogged down, doing the science and engineering. He wrote about how some people may disapprove of black boxing analogies that attempt to understand biology like computing systems and noted that the synthetic biology community ought to "create a framework within which all these different points of view can come together, discuss and shape the future of the field."

The human practices document also addressed and justified work specifically in The E.Ncapsulator, explaining that the team was conscious of their work being "perceived as somewhat 'risky'" in its implication that humans should ingest medications that have been made by a genetically engineered *E. coli*. Mindful of the risks, Andrew explained that the team "built in strong safety measures… right from the beginning". Though I won't go into much further detail, this document shows the beginnings of what turned a simple human practices exercise (that was largely neglected by students and advisors) into a real selling point for this team's overall project. The following chapter goes into detail about the selling of human

practices at the Jamboree. And yet, imperfect as it was, I believe there was a good deal of value in the students' participation in the workshop and interviews – I think they had a chance to engage with a broader set of questions that made them think about their work differently, if only briefly. In this chapter, I shall shortly leave the human practices results topic, just mentioning a few more things about the other document that was added to the Wiki.

The other document, 'Synthetic biology and bioethics', was written by Andrew and his friend who studied philosophy (Appendix III). Though I did not oversee this document at all and believe it shows a puzzling use of medical ethics as it evaluates elements of the iGEM project according to principles of the Belmont Report[125], it did show Andrew's further interest in these broader questions. This document included a section titled 'The scientist and the layman' that covered how the promise of synthetic biology both inspires *hope* for a better future through biotech innovations but also *fear* of scientists 'playing God' or doing something destructive. The writers also commented on biosafety measures taken in the E.Ncapsulator such as using laboratory strain *E. coli* that could not survive in nature as well as in implementing the genome deletion module. Finally, in a confusing section on moral and philosophical implications the writers discussed the open matter of whether synthetic biology constitutes an affront to "the sacred nature of life". They wrote:

> One cannot deny the fact that synthetic biology will change the way people see life. For decades now, everyone has linked the vague concept of "life" to DNA and genes. Now, however, the limit between life and objects becomes blurred, and we no longer have a scientific theory on which we can build our representation of what life is. *Life* is

[125] The Belmont Report detailed ethical principles and guidelines to protect human research subjects in the US (Office of the Secretary 1979).

> no longer in the genes, because the genes have become just another object we use in engineering. It is up to philosophers to redefine / recreate the concept of "life" – or at least to ease the acceptance of the fact that such a thing as *life* simply might not exist.

While I quarrel with this document, I also find it interesting that Andrew's friend – a philosophy undergraduate studying in France – probably spent more time thinking about and writing up this piece than some iGEMers did in participating in the workshop and interview.

Potential futures

I've already mentioned that key sections of the overall project vision were not achieved – cellulase wasn't made; the thermoinduction switch was relatively unsuccessful; the genome deletion module didn't really work; and several tests failed to yield meaningful results. In this section, I shall say a bit more about missed goals before examining elements of The E.Ncapsulator that were deemed as having further potential. Obviously, the first missed goal was attributed to a small human error of sorts – not writing in the correct code of nucleic acids could have been the mistake of a simple one letter typo. In the thermoinduction part of the project, it was relatively unclear as to what went wrong. With respect to genome deletion, John told me that this was unsurprisingly such a "challenging proposition… because you are dealing with something that is lethal" – it was incredibly difficult to time the engineering of a 'cell suicide' because "if you have any leaky expression, everything just dies".

Yet, it is essential to remember that this team set themselves an almost impossible task:

> It was quite an ambitious project – you know, it was looking at a manufacturing process from beginning to end. The design was conceptually quite sophisticated, which always makes delivering something that works essentially way beyond the limit of what you can do in iGEM. – John

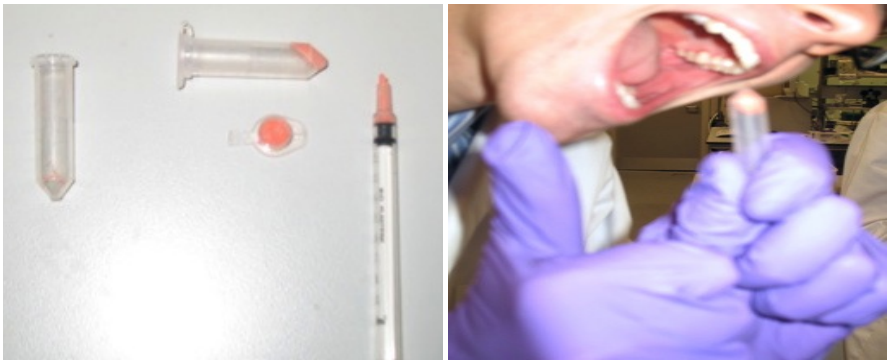
In several cases, success proved elusive in the wet lab, and consequently the engineering cycle as practiced at Imperial College was not fully realized. That is, *real experimental data* – that would ideally be fed into modelling and simulations to, in turn, improve further rounds of experimentation and superior data collection (as in the engineering cycle ideal) – was not gathered.

> The difficulty is having meaningful integration of the modelling into this design process. I think there is an engineering framework to the whole design process in the way that the team abstracted it and had linking modules. But, in terms of actually modelling that, and the modelling being able to influence the design – that is really difficult because that is really a second cycle kind of process. And, in iGEM, you never really get to that second cycle. You are lucky if you get close to the end of the first. So, that is always quite difficult. Because then you just do modelling in abstract – you don't get the data to feedback into model to then feedback into the design. – John

The above quote suggests that modellers, in the end, were encouraged to 'plug and play' with hypothetical data input into their preconceived mathematical equations so that the team could reference possible scenarios in selling the project. In spite of experimental setbacks, the students never rested and kept experimenting at every chance they could (for many, this was between classes and during evenings and weekends as the next school year began). A couple students came up with an idea for "the triple hack" and attempted to build additional layers of coating protection on top of the colanic acid; unfortunately, the genetic materials weren't received quick enough to complete the experiments before the Jamboree. In times

of waiting during routine protocols, students devoted themselves to playfully creating capsule-like forms that they thought they might be able to mock-up as the pill-like forms for E.Ncapsulated drugs (Figure 5.11).

Figure 5.11: Playing around in the lab



Finally, I'll briefly note what the advisors believed were elements of this team's work that merited future research. Roger was particularly keen on encapsulation:

> I think the bit that we are interested in is the encapsulation program – it is quite an interesting concept for all sorts of reasons. For manufacturing of products really… Where you could use this to trigger the encapsulation and protection of products or something. I don't know yet. But, it just sounds intriguing, interesting enough to take forward and explore more.

John was slightly more reluctant about encapsulation's feasibility, unless there were significant additions in further investigation:

> It's a nice idea, a nice project – but it is very difficult at this stage to make a realistic assessment as to how achievable it would really be. You know, would the colanic acid really provide enough resistance to deliver active proteins to the intestine? I don't know. I like the system they've come up with but I think just the colanic acid on its own is probably a no. But if the colanic acid can be fixed on other layers as they've proposed,[126] then I think that would help significantly and it may be possible to some extent. But, you're never going to deliver 100% active product to the intestine through the stomach – you're always going to have a pretty big drop off. So I think you'd have to

[126] This is alluding to the idea of "the triple hack" which was proposed too late in the summer to be completed for the Jamboree.

> pick your target quite carefully – what you actually want to treat. Issues in terms of dosage and control are quite tricky too... And also taking something like that through to market is probably pretty difficult – you know, the regulatory controls would probably be a minefield.

Other elements of the project perked the interests of advisors to varying degrees:

> I would quite like to get one of the master's students looking at that cell death module. Because it is obviously a very important component in terms of synthetic biology – being able to program cell death is actually really important – but it has to be really robust. You've obviously got really high selective pressure against activating it. So it is quite tricky. – John
>
> The trigger programming, where you monitor metabolites and move from one metabolite to another and trigger a kind of control through that. Trying to model that properly – I think that is an interesting idea, where you use growth media to trigger signals, which allow different functions to be turned on in a bacteria. I thought that was good. People have used that before but not in synthetic biology. – Roger
>
> I would say the auto-inducible medium should be taken forward. There should be a further characterization of the thermoinducible promoter. I'm still not sure we'll have a good idea of what colanic acid does. This year, we'll have 12 MRes students and I think that some of them are going to be assigned various aspects of the characterization. Likewise, the IPTG induced promoter – the conversion of LacI – should be another project. These should be given out as MRes projects… Because we have interesting data but they are not conclusive. For iGEM, you can do an experiment once or twice but for somebody who looks at data – like I do – there's no proof in that. It is good enough for the Jamboree but it is not good enough for science. – Pierre

The reader should note this instance where iGEM ideas are used as a starting point for further research; this will come up again more generally in Chapter 7. There are other ways for projects to live on – I've mentioned already how BioBricks get submitted to The Registry and used by future teams in any number of unknown ways; papers are written too, leaving iGEM legacy in prestigious scientific

journals.[127] For Max, publication seemed like the best possible future pursuit for the E.Ncapsulator:

> I think encapsulation is an interesting idea. But, in terms of protein drug production – I am not sure. I mean it is very early days – we are years and years off that. I don't think it would really be a viable PhD or anything like that. I think there will be at least MRes projects from this iGEM project. I guess the end game for us would be to get a research paper out, rather than any kind of product. A lot of research papers can come off the backs of iGEM projects. For example, there is the cancer sensing stuff, an early paper by Chris Voigt. So this kind of thing can get published.

To foreshadow the argument of Chapter 7 – that iGEM is a key tool for assisting the development of synthetic biology – note Pierre's comment:

> As very often with iGEM projects, they just scrape the surface – and someone has to do it properly and more rigorously… As a policy in our department, we take iGEM projects forward. Two years ago we had the cell-free systems and bacterial sensors and now Max is doing it as a PhD. Last year, the *B. subtilis* project got split into two MRes projects. The project from three years ago unfortunately was not pushed forward but that was because there was no real synthetic biology activity here.

Conclusion

This chapter has shown what elements of E. Chromi and The E.Ncapsulator were actualized in some functioning material form, what elements remained hypothetical and where sections of the projects perhaps showed potential for future development. In Chapter 4, one appreciates how much of synthetic biology's core engineering principles – e.g. that discrete parts, devices and systems can be black boxed, each level separable, modular and connectable as Lego™ – fail at the level of experiment. In the wet laboratory, practitioners face

[127] For example, some reputable publications highlighting iGEM projects are Check 2005b; Levskaya *et al.* 2005; Brown 2007; Peccoud *et al.* 2008; Smolke 2009.

natural complexity that resists this engineering ideal. So, when iGEM teams are faced with limited time, skill and resources to complete their projects, they are forced to think creatively about how to prove the *theory* of the project when evidence of *real* results is not delivered. This theme continues to be relevant in the next chapter when I show how teams must *spin* and *sell* their (rather incomplete) projects. Yet, these two teams both constructed some functioning parts of synthetic biological systems[128] – among several accomplishments, just consider the success of Eleonore's violacein construct that clearly yielded purple- and green-producing *E. coli* (Figure 5.2) or the Imperial College team's colanic acid-coated bacterium (Figure 5.8) that was not only viewed convincingly under EM photography but also tested with respect to having a higher acid resistance and protective effect on the cell than the non-coated control specimen.

In conclusion, I'd like to bring these accomplishments into a philosophical debate about the status of scientific thought and phenomena – that is, to ask what kinds of hypotheses and entities are real, or true. And, how can we judge them to be so? Following Hacking's (1983) position, I claim that although we cannot, at this stage, take synthetic biology's theoretical postulates to be true, we can think of some (albeit limited) of its entities as *real* forms of living material with causal powers. Hacking (1983) writes:

> Experimental work provides the strongest evidence for scientific realism. This is not because we test hypotheses about entities. It is because entities that in principle cannot be 'observed' are regularly manipulated to produce new phenomena and to investigate other

[128] One might note that Knorr-Cetina (1983) highlights a similar point that is found in several laboratory ethnographies: the everyday, mundane preoccupation of lab scientists is that of 'making things work', that is, getting machinery, laboratory specimens, etc. to perform successfully and trying to avoid yet another experimental 'failure' (120). For the students and advisors involved in iGEM, they are not really concerned with 'making things real' or claiming the discovery of new scientific 'facts', rather, they are focused on the pragmatic problem of 'making things work'.

> aspects of nature. They are tools, instruments not for thinking but for doing. (262)

Over the last three chapters, I have shown how iGEMers transition from using tools for thinking (mind maps, online forums, etc.) in dreaming up ideas to using tools for doing (synthesized DNA segments, BioBricks, PCR machines, etc.) in actually making new biological phenomena. In the former, we have good reason to doubt the truth of imagined project ideas (or believe that they will work); still, from this doubtful stage of thought, eventually real materials, with causal and measurable properties, were born. Further, the ways in which materials such as the violacein-carrying *E. coli* might live on in experimenting, connecting and interfering with other parts of biology are extensive – a major objective behind BioBricks being openly shared. Perhaps in the future these colour-producing constructs will not only connect to biosensors, but also other yet imagined biomechanical devices.

Hacking (1983) believes that experimenting is about 'creating, producing, refining and stabilizing phenomena' (230). In his example, he argues that we ought to believe in the reality of electrons because of experiments in which electrons are used to interfere and cause other things to happen – for instance, in spraying nobium balls. He declares, "so far as I'm concerned, if you can spray them then they are real" (ibid, 23). Similarly, when Eleonore took the freeze-dried violacein DNA sequence (synthesized from scratch) from its FedEx package, worked it up in a series of experiments and then introduced it into live *E. coli* cells in three different forms (one was the full construct, the others had part of the sequence excised) to finally generate violet- and green-producing bacteria – we have good

reason to trust the reality of this construct. There is something created, produced, refined, used with intentional cause and effect behind the entities named BBA_K274002, BBA_K274003 and BBA_K274004[129]. Finally, I would add that my position strengthens if, in future, we see these BioBricks functioning inside other biological machines.

> Reality is bigger than us. The best kind of evidence for the reality of a postulated or inferred entity is that we can begin to measure it or otherwise understand its causal powers. The best evidence, in turn, that we have this kind of understanding is that we can set out, from scratch, to build machines that will work fairly reliably, taking advantage of this or that nexus. Hence, engineering, not theorizing, is the best proof of scientific realism about entities. (Hacking 1983, 274-5)

In Chapter 1, I noted the social constructionist position:

> Facts and artefacts in science, as well as what we think we know about them, are, according to some social constructionists, actually 'social constructions' tied into a matrix of people, ideas, institutions, practices, hierarchies, politics, etc. – without inherent truth. Therefore, a social constructionist might say, there is nothing 'special' about scientific knowledge and practice that should separate it from 'the social', nor other forms of knowledge production.

Of course, in Chapters 3 through 5, I have shown how team dynamics, hierarchies, role-playing, competitive motivations and several other social constructions were at work as these iGEMers pursued their projects. However, just because social constructions are operating (as they do *everywhere*), it need not conflict with a position that believes *real*, functioning synthetic biological forms can, and have been, created. When parts of biological machines succeed in fulfilling designed functions (albeit rarely), we also have reason to believe that additional products and applications might arise from synthetic biology. These potential future living machines will undoubtedly interact with people and the environment in currently

[129] These are the violacein BioBricks (http://2009.igem.org/Team:Cambridge/Project/VI02).

unknowable ways. It seems sensible, however, that we deem these synthetic biological entities as having a status other than social construction so that we (especially those investigating this field from a humanities perspective) continue to interrogate their constitution and causal powers with technical rigour.

How might we think of, name and categorize synthetic biological machines? Are they machines, organisms or a hybrid of both? Shall we even consider these completely new forms of *life*?

> The problem of the relations between machine and organism has generally been studied only in one direction: almost always, the attempt has been to explain the structure and function of the organism on the basis of the structure and function of an already-constructed machine. Only rarely has anyone sought to understand the very construction of the machine on the basis of the structure and function of the organism. (Canguilhem 2009, 75-6)

Interestingly, the experience of many synthetic biologists contradicts Canguilhem.[130] I've heard a great number of synthetic biologists explain that the living kingdom is an inspirational source of the most magnificent machines – DNA in a given organism encodes instructions for the functioning of vast numbers of proteins, reactions and phenotypes. Hence, synthetic biologists seek out patterns and regularities in biology that afford various forms of production in repeatable and robust ways. They want to not only replicate those patterns, but to make them better, more refined in their own re-designing, re-sequencing, re-synthesizing of DNA for specific mechanical functions. Many synthetic biologists construct their machines today on the basis of the structure and function of organisms.

[130] Note that the quoted passage was originally published in 1952 in *La connaissance de la vie*.

According to Canguilhem (2009), a machine is "an artificial construct, a work of man, whose essential function depends on mechanisms" (76). He continues:

> A mechanism is a configuration of solids in motion such that the motion does not abolish the configuration. The mechanism is thus an assemblage of deformable parts, with periodic restoration of the relations between them. The assemblage consists in a system of connections with a determined degree of freedom… The material realization of these degrees of freedom consists in guides – that is, in limitations on the movements of solids in contact. In any machine, movement is thus a function of the assemblage, and mechanism is a function of configuration. (76-7)

Consider how synthetic biological machines do and do not fit this thinking:

- They are man-made, artificial constructs – but they are also constituted, and inspired by, natural biological phenomena.
- Their function depends on mechanism – but also on the materials and processes of living organisms (e.g. gene transcription allows a given biological machine to fulfil its purpose).
- The mechanism depends on an assemblage of deformable parts: BioBricks.
- Practitioners of synthetic biology would ideally like BioBricks in their systems to connect with a determined degree of freedom – but this is rare, as numerous biological complexities are constantly at play.
- Movement in a synthetic biological machine will be a function of the assemblage – but there will also be a number of unknown and uncontrollable movements happening due to the noisy, stochastic nature of biology.

Using Canguilhem's (2009) sense of the differences between machine and organism, we can continue reflecting on the ambiguity of classifying synthetic

biological organisms as *machines*. For instance, he goes on to discuss how machines have "geometrical, measurable displacements" (ibid, 77); how they are "strictly the sum of the parts… [displaying] functional rigidity, a rigidity made increasingly pronounced by the practice of standardization" (ibid, 88); he talks about the uniformity of metric and qualitative characteristics that allows interchangeability and equivalence of parts of the same kind (ibid, 88). By now, it goes without saying that these mechanical qualities are clearly elements that synthetic biology *theoretically* strives for; however, experimental realities are mostly far from this mark. *Though possible, it is very difficult to turn organisms into machines.*

In an organism, by contrast, Canguilhem (2009) writes that "one observes phenomena of self-construction, self-conservation, self-regulation, and self-repair" (88) and such sophisticated functioning means that organisms must possess "a plurality of functions" (90). Organisms, for Canguilhem, have "greater latitude of action than a machine… less purpose and more potentialities" (ibid, 90).

> The machine, which is the product of calculation, verifies the norms of calculation, that is the rational norms of identity, consistency, and predictability. Life, by contrast, is experience… improvisation, the utilization of occurrences; it is an attempt in all directions. (ibid, 90)

Furthermore, the living world creates monstrosities and, in Canguilhem's view, "there is no machine monster" (ibid, 99). But will this be true of future synthetic biological machines? Will synthetic biology generate systems that may be perceived as mechanical monsters? Though colour-producing bacteria are unlikely to offend most people's moral conscience, perhaps ingesting drugs that are produced by a genetically engineered *E. coli* starts to be unsettling.

Design interactions work around synthetic biology provokes viewers' reflection on the acceptability of imagined potentials in a future world of synthetic living machines. In Daisy Ginsberg's video, *A Natural History of the Synthetic Future*, she asks the currently unanswerable question of how synthetic biology practitioners might control unknowns as biological machines endeavour to get increasingly sophisticated. She also asks how we will classify what is natural or unnatural when life is built from scratch and wonders whether the simplification of life to its molecular mechanics might "accidentally degrade our sense of self".[131]

In my view, it is not yet time to jump to categorical conclusions, not least because synthetic biology is at such a formative, uncertain stage in defining and delivering on its proposed theory. Rather, it is time to open out an informed space for questioning. This thesis has come to a critical stage, having shown several aspects of day-to-day workings of synthetic biology practitioners, giving insights with which to start reflecting on matters in the debate around engineering life. What are the promises of synthetic biology and, crucially, do we see evidence for believing them? What is actually possible in engineering living systems? Is this safe, sound and morally acceptable – and to whom? Who should judge and regulate how synthetic biology continues to develop its tools, techniques, products and applications such that the field is responsible and accountable with respect to social, ethical, legal and political concerns? Those interested in how this debate continues must inform themselves, raise questions and act in the present if they are to help shape the future of synthetic biology's interaction with broader societal contexts.

[131] http://www.daisyginsberg.com/projects/syntheticingdom.html.

The next chapter moves into a new section of empirical data taken during the iGEM Jamboree, where I explore not only the Cambridge and Imperial College teams' experiences, but also sociological aspects of the international synthetic biology community. Thus far, I have presented a picture of two microsocial circles in which iGEM teams conjured up intriguing ideas, faced challenges of turning thought experiments into real experiments and found some triumph in making new and interesting parts for biological machines. I have also shown how the teams went some length in reflecting on synthetic biology's implications (in design workshops at Cambridge and in the human practices exercise at Imperial College). The kind of close ethnographic examination that I've offered is currently lacking in other synthetic biology commentary and it is my hope that this grounding in an actual narrative – with real characters who were authentically attempting to follow and define ways for constructing biological machines – is helpfully adding to a more informed position to take as debates around engineering life continue to unfold.

6. SELLING IDEAS

From late August until the Jamboree (30 October - 2 November, 2009), both teams slogged through long hours constructing presentations and posters, knowing that their efforts would soon culminate in highly competitive stakes. Both teams had the reputations of their universities to uphold on the international stage, in addition to pressures to excel for their advisors. Such pressure would be natural after months of intense learning and assistance from advisors, who would act as referees for students in their later educational and career choices; moreover, many students simply wanted to do well out of gratitude and respect for their teachers. Pressure to succeed for advisors (and the institution) was implicit at Cambridge where instructors often voiced their pride in the team, regardless of outcome at the Jamboree, as they neared the finale. At Imperial College, however, the pressure *to deliver* for *the whole team* (including advisors) – and also the reputation of the newly formed Centre for Synthetic Biology and Innovation (CSynBI) – was much more explicit. Advisors insisted that the team up their game for the competition: Imperial College has status as a *winning* institution.

Exhausted yet still driven to succeed – especially since they had come this far – both groups realized that after all their dreaming up ideas, struggles in experiment and attempts to make new functional biological systems, their next big task was to *sell* their projects. I won't belabour the lead-up to the Jamboree much further, but it is important to point out that the Cambridge team's presentation was perfected over the course of several gently critiqued practice sessions, as well as at another design workshop with James King. Given the Cambridge advisors' experience in

previous competitions (where some of them were judges), they were very useful in nudging students towards refined presentation that ticked the right iGEM boxes. James' eye for sleek yet playful design, his probing questions about possible futures for the project's colour-producing bacteria as well as lending the team the E. Chromi logo[132] (designed by James and Daisy) further helped students craft their presentation. The Imperial College team also practiced and refined their presentation, as they persisted through several critiques to perfect their selling tactics right up until the moment they took stage.

This chapter takes the reader into a new setting, mostly at MIT (Cambridge, MA, US), where members of various synthetic biology communities, from all corners of the globe, met for three days of what some refer to as *the Olympics of amateur genetic engineering*: the iGEM Jamboree. The first section sets necessary context. I then discuss how ideas were sold: this concerns not only how students sold their projects, but also how highly recognized figures of synthetic biology pushed enticing philosophies and future visions. Ideologies of sub-communities such as DIYbio were on display as well. Views on good and evil biological practice from Federal Bureau of Investigation (FBI) agents were presented. And, a new role for art and design in synthetic biology was being sold too.

6.1 Setting the scene at the iGEM Jamboree

Arriving in Boston on Thursday, October 29, 2009 (a day earlier than the iGEM teams I was following, so I could do some initial solo scoping), I was extremely

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132  (http://www.echromi.com/).

excited for this pinnacle event in my research that would inevitably expose me to a bigger and more complex picture of synthetic biology's social world. Armed with recorder, notebooks, several back-up pens, batteries and camera, I was determined to absorb as much as I possibly could in four days. I had no idea how intense this weekend would turn out.

Getting settled in my hotel, I found that Randy Rettburg (Director of the competition) had emailed me asking if I'd be willing to help with the judging process.[133] I immediately called him and though I was not asked to be an official judge, Randy wondered if I would help judge the judging; this "meta-judging", he explained, aimed to examine issues of fairness and think about ways to improve the competition's judging standards. I agreed to keep watch for such issues and report back to Christina Smolke[134] (in charge of meta-judging) with any interesting findings. This was an excellent start: I'd been included as a working member of the iGEM community; I'd be able to speak with several key players in the judging circle; and, I'd try to uncover issues of unfairness, which was a problem in the competition's politics. All the while, I would be informally speaking with iGEM teams and stakeholders, just as I had hoped.

I decided to spend Thursday evening strolling around MIT and Harvard, getting a feel for the setting and thinking about how to strategize for the weekend. The MIT campus is a hub of innovative engineering, with the outstanding Ghery-designed Stata Center being the heart of much of the weekend's action (Figure 6.1). Inside

[133] I emailed iGEM Head Quarters prior to the competition, explaining my research and asking if there would be opportunities to get further involved 'behind the scenes' at the competition.
[134] Christna Smolke is one of very few female elite synthetic biology professionals, holding one of the most impressive CV's in the field: http://openwetware.org/images/1/1a/CDS_CV.pdf.

the Stata Centre's bold and bright architecture, plenty of light and chalkboards line the hallways. I wrote in my field-notes that this space seemed "like a cross between a playground and a spaceship", certainly inspiring a sense of wondrous curiosity on its own, let alone with the addition of hundreds of keen, aspiring bioengineers, showing off their biological machines. A few subway stops away, I found myself gazing at Harvard Yard's pristine red brick buildings and perfectly symmetrical walking paths in the main square, watching students shuffle in and out of evening classes and the library. This was land of the Ivy League. I'd also comment that the Jamboree's timing added to the incredible atmosphere: it was Halloween weekend; jack-o-lantern pumpkins and monsters decorated the well-groomed streets; brilliant red and orange foliage littered the landscape, the air was crisp, seasons were changing. After a few solo hours of wandering, I sat in my hotel lobby, watching iGEM teams from all over the world check-in – some noisy and animated, others reserved or simply exhausted from long-haul flights. It would all begin tomorrow, I told myself.

Figure 6.1: The Stata Center

The Jamboree package pick-up and schedule didn't start until Friday evening, so I packed the day with meetings and investigating. Firstly, I set out to Pamela Silver's laboratory in the Department of Systems Biology at Harvard Medical School[135]. There, I met a PhD student in synthetic biology, Claire (pseudonym), who was involved in iGEM as an advisor and judge and whose interests ran through bioenergy, social studies of science and bioart. Claire and I had arranged to meet after she responded to a posting that I placed about my research on the DIYbio online forum[136] and we exchanged a few emails. When I arrived at the Medical School, despite the building's sterile exterior, the actual laboratory had a very warm feel to it, with pale wooden shelves and desks, cluttered benches that were decorated with people's photos and some quiet background music. Claire was immediately likeable. After a bubbly and enthusiastic welcome, we decided the first order of business was a lab tour. I was shown the heavy machinery room with its massive centrifuges and other equipment that resembled industrial-sized washing machines; there were also several large gas tanks and elaborate tubing systems (as this laboratory specializes in bioenergy). I was then introduced to a few PhD's and post-docs, given brief introductions to their work, and was struck by the much higher proportion of women in this lab than I experienced at Cambridge and Imperial College. To my delight, I also met Pamela Silver, who was rushing off to a meeting, but still took time to tell me about her laboratory's over-arching bioenergy theme that emphasized understanding the underlying

[135] Pamela Silver is another notable female leader in synthetic biology (along with Christina Smolke): http://silver.med.harvard.edu/; http://openwetware.org/wiki/User:PamSilver.
[136] A link to my posting: http://groups.google.com/group/diybio/browse_thread/thread/3068730dc7c7ca57/c8686c7a8d3b86c1?lnk=gst&q=Caitlin#c8686c7a8d3b86c1.

biology. Pamela reminded Claire, "make sure you show Caitlin the fish"[137], then she was off.

I return to my discussion with Claire in the following chapter, and now briefly describe the interesting meeting I had later that afternoon with Sam Gaty and George Costakis, documentary film-makers from Portland, Oregon. Again, Sam and George contacted me after I made the posting on the DIYbio forum; they wanted to discuss our mutual research interests in telling "an honest story of what's going on in synthetic biology". Sam and George were at the 2009 Jamboree to do some initial research, before they set out to film in 2010. In an email, they described their work's aims and wanting to meet with me:

> We are not interested in making a sensationalized or hysterical film about the terrors of genetic engineering or synthetic life. The goal is to simply explore where these technologies are and what they are capable of doing. The film should be educational and engaging, intended for a general audience...
>
> We read your posting on the DIYbio Google group which included a summary of your research and interests, all of which seem to be very in line with the goals of our proposed project. Your research sounds both interesting, and useful in informing how our project develops. If you have time while in Boston, it would be great to sit down with you and talk about our project and your research…

The meeting with Sam and George was enjoyably casual, as I highlighted some of my experiences in being embedded with synthetic biologists and they asked questions. It was slightly odd too to be more an interviewee, as opposed to my usual interviewer position. In Chapter 7, I'll point out where Sam and George's work has progressed.

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[137] I later saw the fish. Claire explained, "we have this strain of cyanobacteria that we are injecting into fish embryos in order to engineer photosynthetic fish. It is sort of more *early stages!* But, it works – they don't die! And that's the goal, sort of". There were several points of interest at this laboratory but one I'd like to highlight is that although these practitioners include themselves in synthetic biology's 'engineering approach', at that point, their focus remained on understanding the complex cell biology that underpins the engineering work of the more distant future.

The countdown to absolute Friday night frenzy at the Stata Center was nearing as masses of iGEMers gathered to pick up their team's weekend Jamboree packages, eat pizza, drink soda and practice their presentations[138]. I received a text message from Andy, telling me that the Cambridge team had arrived and were heading for a tour of the Stata Center. I met the team – who were clearly exhausted, excited and nervous – and we set out for a guided march around MIT, led by Andy, who had attended three previous competitions and worked at The Registry one summer.

The Registry of Standard Biological Parts is housed in the shared office of Tom Knight[139], Randy Rettberg[140] and Meagan Lizarrazo[141] (among others), within MIT's Computer Science and Artificial Intelligence Laboratory (CSAIL). Tom Knight and Randy Rettberg are well-regarded figures of the AI and computer science worlds, having developed several important tools and technologies in that field since the 1960s, as well as having been integral in developing the Internet. These guys are *a big deal*. Given that Andy, Samuel, Geoffrey and Frederick are friendly colleagues of Tom and Randy, we simply walked straight into their office – only a couple hours before the Jamboree, so one can appreciate how busy these people might have been. The tour was quick but seeing the setting and actual Registry of BioBricks was fantastic (another perk of being with a VIP team). The Knight Lab was messy and completely bizarre: papers piled high on most desks; an interesting mix of computer, physics, biology, maths, engineering and science

[138] Some teams registered beforehand for a limited number of practice slots on Friday evening that allowed access to the actual big auditoriums they would present in 'for real' later that weekend. Neither the Imperial College nor Cambridge teams decided this was necessary.
[139] Tom Knight is the creator of the BioBrick concept and a Senior Research Scientist at CSAIL.
[140] Randy Rettberg is Director of iGEM and a Principal Research Scientist at CSAIL.
[141] Meagan Lizarrazo is the assistant Director of iGEM.

fiction books lined wooden shelves; on top of old filing cabinets were relics of computer engineering, such as massive motherboards and floppy disks larger than the size of a full modern-day laptop. Oddly, it looked as though this office was caught in the 1970s, despite housing what is talked about as a 'cutting edge' repository of standard, interchangeable BioBricks that are meant to be the starting materials of a future generation of biological machines.[142] Our tour highlight was also strangely anticlimactic: the *real* freezer (as opposed to the online repository) that now holds almost 15,000 BioBricks[143] that have been contributed to The Registry through iGEM (and, to a lesser extent, other laboratories) was really *just a large and extra cold freezer* – no bells and whistles – and it was oddly situated in a cramped corner, tucked behind some bookshelves and the otherwise dry lab office space. Figure 6.2 shows Tom Knight opening up The Registry freezer for Daisy Ginsberg.

[142] Meagan's work area was the exceptional space – tidy and organized.
[143] This number was cited by a key speaker (13 April 2011) at The Royal Society and The Royal Academy of Engineering meeting on 'The economic and social life of synthetic biology' (http://www.raeng.org.uk/events/pdf/syn_bio_programme.pdf).

Figure 6.2: The Registry Freezer

Credited to James King.

We cleared out of the Knight lab and Andy continued touring us around interesting nooks of the Stata Center – the rooftop view, the bar, the synthetic biology hang out areas, the place where he occasionally slept while he was working for The Registry. It was then time for everyone to head to the designated room to pick up registration packs. The second photo in Figure 6.3 illustrates the Jamboree packs, stacked like bricks, for over a thousand participants. I stood with the team in a lengthy, cramped queue and discussed the days ahead as we all soaked up the energy of loud, eager teams. I still hadn't heard from the Imperial College team and the Cambridge clan were about to head out for dinner after grabbing registration packages, so I decided to stay for the Friday evening session of pizza, pop and practice in the Stata Center, hoping to meet other teams.

Figure 6.3: iGEM Jamboree 2009 begins

Photos attributed to iGEM and David Appleyard.[144]

As I wandered about the Stata Center's corridors on the eve of the Jamboree, the spectacle really began to take shape. Teams found their own little corners – alcoves with benches and desks are a convenient feature of Gehry's asymmetrical architecture – in which to eat, sleep, practice presentations and invite others to chat. The chalkboards began to get filled with artfully drawn team logos, cartoons and selling slogans. Students lifted their smallest team member onto the shoulders of the tallest in order to get every bit of blackboard space filled in. These blackboards, in fact, became (and have remained) one of the symbolic images of the Jamboree – in Figure 6.3 note that the first photo (left, by David Appleyard) became the cover of Nature Biotechnology's December 2009 special issue on synthetic biology (right).[145] That evening, I talked to at least a dozen different teams about their projects and iGEM journeys – notably, I recall student-led Osaka team's enthusiasm.[146] I was drawn to this team when I saw their poster, propped up on the table as they ate and slept in an alcove of the main atrium. The poster had

[144] These and other photos in chapters to come that are attributed to iGEM and David Appleyard are sourced from: http://www.flickr.com/photos/igemhq/sets/72157622736773466/.
[145] Cover credited to Kim Caesar, based on David Appleyard's photo. Nature Biotechnology, December 2009, Vol. 27 No. 12: http://www.nature.com/nbt/journal/v27/n12/covers/index.html.
[146] http://2009.igem.org/Team:Osaka.

incredible photos of colourful plates and, talking to the students, I discovered that their project was based around creating new tools for bioart by integrating cell-to-cell communication, colour and motility. All of their artworks (including the titles GFP Paper Bunny, Cocktail, Tomb and Mandala) were made using genetically engineered bacteria, and through this work the team explored biomedia and bioethics in synthetic biology. Interestingly, this group began as a completely student-led team, who then had to recruit an advisor to meet the iGEM requirements; they also told me that not a lot worked out in the lab as they hoped, but that they were still able to create some very pretty pictures (I encourage the reader to visit the team's Wiki). I continued to network that evening, introducing myself to several interesting iGEM and synthetic biology affiliates – including members of the UN and FBI, members of the DIYbio community and members of biotech and pharmaceutical companies (seen, to some extent, as rivals the iGEM ethos in its private, corporate and heavily IP-protected research endeavours). Having set the scene, let us now dive into the fascinating story of who had ideas to sell at the Jamboree and how they did so.

6.2 Selling ideas

In exploring content and method behind selling ideas, I shall begin with examples of how iGEM teams presented their projects to judges, hundreds of peers and interested outsiders – with only twenty minutes to shine. On the first morning, I attended a presentation from UC Davis[147] – clearly an underdog team. Yet, their performance was nonetheless exemplary of several trends in Jamboree talks. Firstly, the presenter explained that their project was personally motivated – a

[147] http://2009.igem.org/Team:UC_Davis.

team member described how his roommate had Celiac disease and how "this sucks because he can hardly eat anything". Accompanied by a PowerPoint projection, team members stood in a row, passed the microphone along and described the disease, its negative effects on sufferers' lives, the current treatment (a pill taken before every meal) and its drawbacks. Then came the team's proposed genetically engineered solution: a microbe that would reside in the stomach for at least a month and secrete the necessary enzyme that Celiac-afflicted people do not naturally produce, subsequently ending the need for pill consumption. With the ambitious problem-solution vision described, the team went on to humbly explain that they didn't get very far in the lab. They said, "we kept on getting two mystery bands when we were running our gel. We think something – we're not sure what – was getting in the media". Experimental failures were mentioned in a number of presentations – though one can appreciate that it was also something *not to say* for teams that felt particularly competitive. For certain, after several informal conversations with iGEMers about their project's details, it is reasonable to conclude that almost every team faced significant displacement between their original project vision and what was actually achieved. The UC Davis presentation also spoke about safety concerns – a minimum standard that needs to be met by every team (an additional brief safety report submission is also required). Finally, the UC Davis team also experienced a very negative comment following their presentation – another (occasionally even fierce) element of the competition. After this team's rather endearing presentation, an audience member remarked that the group's conception of the Celiac disease mechanism was fundamentally incorrect, essentially shutting down the entire project idea. Though this criticism may have been true, as I was sat next to

Geoffrey, he leaned over and said, “now that is just uncalled for” – implying that such comments are too harsh for, what should be (but sometimes is not), a friendly iGEM spirit.

Moving to another of Saturday’s presentation highlights, the Imperial College team was up (Figure 6.4’s top row shows the team awaiting their session). The two chosen speakers (the most confident salespeople of the team) conducted the performance and their articulate, strong delivery was apparent – their audience listened attentively. The talk was a compelling initial problem-solution pitch that then took the audience through each module of the engineering approach in their encapsulated, drug-manufacturing system. An unfortunate point, however, was that the presenters were, at the last-minute, specially coached by Bernard to ‘ramp up the selling points’. A bit of an ‘old-school’ character, Bernard advised that the students address the audience as “ladies and gentlemen” and really emphasize the emotive messages – saying things like “these are children we are talking about here!” when talking about possibly curing PKU. Though uncomfortable with such a cheesy sales pitch style, the students respected their advisor’s advice and presented with this added spin. I heard several whispers following this presentation and witnessed a few eyes rolling, reflecting feelings that the sell was a bit excessive.

Interestingly, the Imperial College team faced scrutiny from a leading human practices stream judge in the Q&A period. The judge urged a further explanation of the impact of the team’s human practices work, to which one student answered: “the genome deletion module was a direct consequence of doing the human

practices project". This was actually not true (as the genome deletion module had been thought of prior to the human practices exercise), though it did seem to work as a selling line. The same judge also noted that he was unable to access one of the links on the human practices page of the team's Wiki. At that point, I recalled, only weeks earlier, experiencing frustration in finishing the film editing, producing a summary document and making a brochure with little help from anyone except Andrew (and he too was experiencing mounting pressure from above to work on the more important tasks). I had been disappointed when the gesture of getting the human practices work online was not completed properly – and now the team was being called on this error by a judge in their presentation. Despite these hiccups in the team's presentation, it remained clear that they had a rigorous engineering approach in conceiving, constructing and testing (or, at least attempting those last two stages) their biological machine and their work stood out as an obvious top-level contender.

For brevity, and to appreciate the diversity of projects represented in iGEM, I summarize a few other presentation highlights:

- The astounding and trail-blazing ArtScience Bangalore team[148] was composed of art and design students, in association with staff at the Centre for Experimental Media Arts (CEMA) and the National Centre for Biological Sciences (NCBS). Describing their project to "engineer the smell of rain" (a scent of special cultural significance in India), the team endeavoured to learn about synthetic biology's tools and techniques while developing a piece of life that reflected their

[148] This was the first team and work of this kind in iGEM (http://2009.igem.org/Team:ArtScienceBangalore). After 2009, art and design continued to play a part in iGEM and in synthetic biology more broadly.

concerns with cultural, ethical and aesthetic implications. The team used a DIY approach to genetically engineer the synthesis of Geosmin, an enzyme responsible for the "earthy rain smell" that is produced by cyanobacteria and actinobacteria. This team also engaged the urban poor and students of design, explaining their artistic involvement with synthetic biology.

- The BioBrick-A-Bot was a liquid handling robotic system made of actual Lego™ pieces (with hardware and software components), designed and amazingly built by an 11-year-old from the University of Washington. Unfortunately, this prodigy was unable to attend the Jamboree due to illness but he sent in a video of his incredible presentation, watched by a completely astounded audience.[149]
- Team Valencia engineered yeast to sense and respond to electrical signals, producing light and showing movement on the first LED bioscreen. They had also done a lengthy literature review, interviews and a comparative analysis of previous iGEM human practices projects, in order to produce a 'Sins, ethics and biology' report.[150]
- The Tokyo Tech team explained their vision to produce bacteria that Terraform Mars. A project to "open new doors for recent space programs" and "stimulate intellectual curiosity about space technologies", this team worked on four approaches to making bacteria that could adapt to, and modify, a Martian environment.[151]

[149] http://2009.igem.org/Team:Washington-Software; for the highly recommended presentation video, see http://2009.igem.org/files/video/Washington-Software.mp4.
[150] http://2009.igem.org/Team:Valencia/home.
[151] http://2009.igem.org/Team:Tokyo_Tech.

- The Berkeley Wetlab team developed an automated approach to large-scale parts assembly that was to be 'accurate, high-throughput, reduced in labour, and decreased in cost', as part of their foundational research project that characterized *E. coli* cell surface display systems.[152]
- Gaston Day (High) School's team of young teenagers worked on a farming issue in their rural community, as they attempted to engineer a microorganism to detect nitrate pollution in water. Incredibly, this team worked with extremely limited knowledge (the most relevant qualification any team member had was a high school course in biology and/or chemistry) and very little laboratory equipment and space. They explained, "We had to think creatively". For instance, this team built a homemade UV light box for $15. Though little was achieved by way of bioengineering, this group certainly learned a lot; they were proud of their homemade equipment; and they embodied great enthusiasm for iGEM, remarking that the team would like to speak at conferences and further pursue synthetic biology.[153]
- Then two-time overall iGEM competition winners (who won again in 2010), team Slovenia presented highly technical work that manufactured nanomaterials by combining modular peptide elements and protein domains, which self-assemble into larger complex structures with designed macroscopic properties. The intriguing point of this team's talk was their announcement that they filed three patents

[152] http://2009.igem.org/Team:Berkeley_Wetlab.
[153] http://2009.igem.org/Team:Gaston_Day_School.

> on parts of their iGEM project. This was met with several huffs from an audience that mostly supports the iGEM's open source spirit.[154]

Finally, I'd like to discuss Cambridge's selling presentation. Like the Imperial College team's session, the full auditorium sprinkled with synthetic biology celebrities signalled that this might be one of the competition's most exciting, prize-contending presentations. Four students shared the presentation's twenty-minute slot that Sunday morning – and though a couple of them began with shakiness in their voices, that quickly settled into clear, calm and well-rehearsed deliveries. The team had the elegant feature of the designed E. Chromi logo but, otherwise, it was real tangible results – vivid colours with data to match – that were the real selling points. This team wasn't encouraged to speak hyperbolically and their modesty made for an even more believable presentation. At the end of their talk and after a full Q&A period, the team decided to sweetly sing happy birthday to one of their embarrassed teammates.

Figure 6.4: Team spirit

[154] http://2009.igem.org/Team:Slovenia.

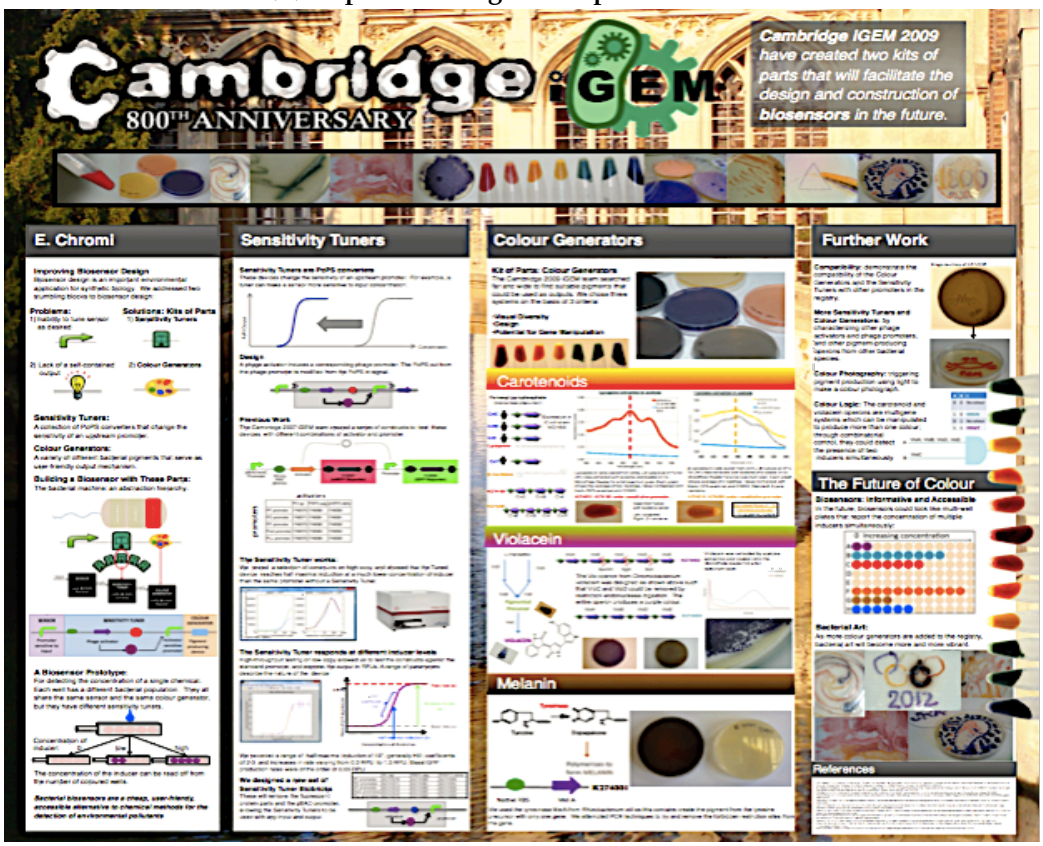
Photos attributed to iGEM and David Appleyard.

Selling projects was of course, not only about that twenty-minute presentation; displaying team spirit and promotional messages was non-stop throughout the competition. Mascots, colourful team T-shirts, matching wigs and give-aways (stickers, toys, business cards, pamphlets, etc.) were all illustrative of how teams further marketed themselves (Figure 6.4). Of course, Wiki's[155] (freely available online to anyone, anytime) and posters (e.g. Figure 6.5) were another space in which to sell ideas, with dazzling images, hysterical video clips and overstated achievements. At every break from the parallel sessions (early morning, lunch and

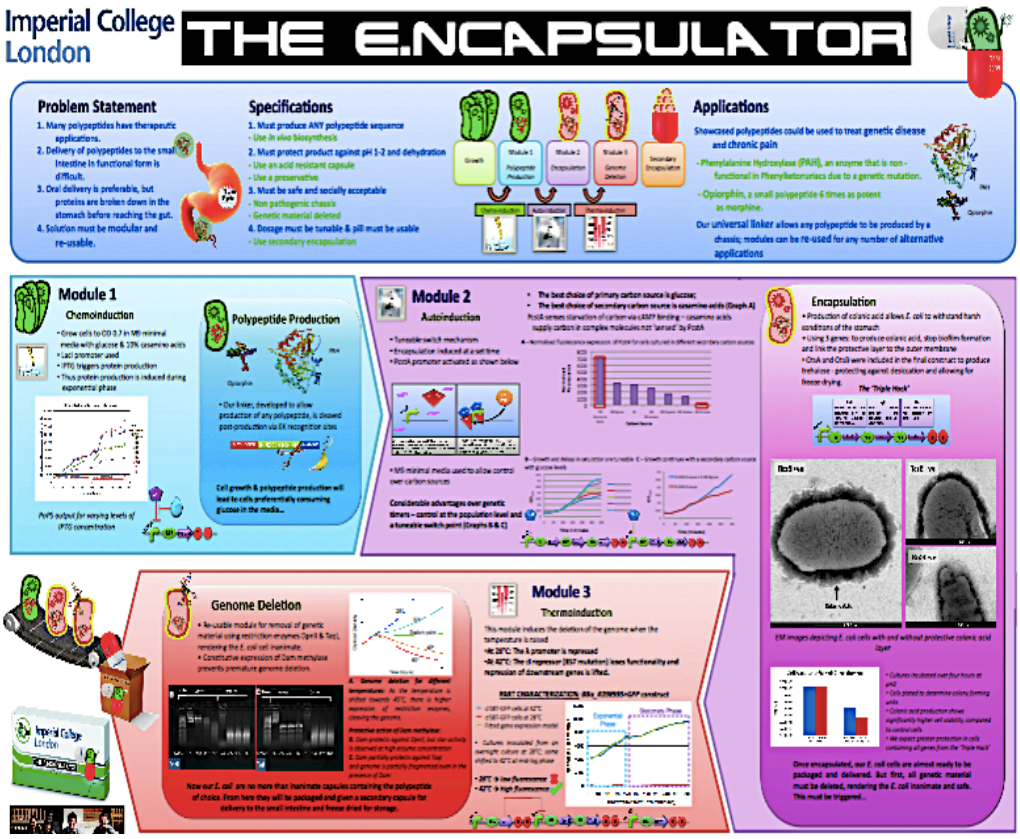
[155] Access to all 2009 iGEM Wiki's: http://ung.igem.org/Team_Wikis?year=2009.

evenings), there were usually a few students at hand alongside team posters (hung in delegated atrium spaces), ready to explain their work to anyone passing by, particularly to judges. At these times, I visited several team posters to hear many more pitches and I had the chance to conduct about ten informal team interviews. I was interested to hear how students described their work and responded to my questioning about an (inevitable) gap between their first ideal vision and what was actually accomplished; I also spent some time asking about students' experiences of judging as part of my input into the meta-judging concern.

Figure 6.5[156]: (i) Cambridge E. Chromi Poster and (ii) Imperial College E.Ncapsulator Poster



[156] Both posters have been cropped, so as not to identify real names of team members.



Turning to another form of performance, it is important to appreciate that iGEM's creators, judges and orchestrators also have *ideals*, which were sold back to students and other players (e.g. the media). There was a sense of preaching *the spirit of the competition* and the virtues of jumping on the synthetic biology bandwagon throughout the weekend. For instance, iGEM leaders raved about the competition in the opening and concluding ceremonies, but it was also not unusual to see the well-known names of synthetic biology floating around the poster sessions, talking to students, as they welcomed in that year's intake and made them feel part of the community. A list of synthetic biology's idyllic philosophies were pushed, by convincing characters, to Jamboree attendees:

- This community embraces creativity and out-of-the-box thinking in a way unparalleled in other fields of science and engineering today;

- This community is revolutionary in its open source ethos that supports collaboration as well as work from amateurs and lesser-funded laboratories;
- This community believes biotechnology will make the world a better, cleaner, healthier place in the coming decades – we are now in The Century of Biology as Technology;
- This community consists in friendly and outgoing contributors whose expertise cross several disciplinary fields – from all walks of science and engineering, to humanities, art and design. This community is not represented by stereotypical images of reclusive scientists; rather, it is represented by a mix of clever, vibrant and playful characters;
- Finally, dedicated researchers who enter this up-and-coming field will prosper financially for their incredible work to come. Most notably, this point came through in the closing speech of iGEM Director Randy Rettburg when he announced, "I think that over the next 40 years synthetic biology will grow in a similar way [as the computer revolution] and become at least as important as the Internet is now and that you will be the leaders, that you will form companies, that you will own the private jets and that you will invite me for rides".

Figure 6.6 helps tell the story of iGEM's community spirit. Pictured first is a scene from Sunday night's Jamboree party, held at Jillian's Boston, self-described as "A 70,000 Square Foot Food Entertainment Universe"[157]; this place was a massive, four-floor, all-American, diner / sports bar / bowling alley / dancehall

[157] http://www.jilliansboston.com/.

combined venue. The iGEMers enjoyed hot dogs, burgers and soft drinks (alcoholic beverages for the strictly carded over-21's), played pool, showed off their bowling arms or danced the night away (well, until that party ended at midnight, as everyone would have to be up for Monday morning's exciting results announcements). Hilariously, the iGEM videotapes that had been rolling all weekend were played on the large screens that plastered the venue's walls – see the scene of happy, jumping dancers with their not-so-distant competition tense expressions in the photo. Figure 6.6's second photo (with the audience being conducted to cheer and do a synchronized wave) was taken on Monday morning as the audience anxiously awaited the finalists to be displayed on the big screen. Finally, the third image was taken at the pinnacle of build up: after all six finalists presented, the judges went into a closed room to make their final decisions as iGEMers were led outside for the symbolic 'iGEM from above' photo[158]. These photos only go a small way to illustrating the exhilarating iGEM energy that was effectively sold and taken up at the Jamboree. There was never a dull moment.

Figure 6.6: An easy sell: membership into the iGEM community

[158] These symbolic iGEM photos have been taken every year to show the growth of competition and display colourful team spirit: http://ung.igem.org/Previous_iGEM_Competitions.

Photos attributed to iGEM and David Appleyard.

I'll now illustrate how associated individuals and groups also had impressions to give, ideals to push and provocations to illicit whilst at the Jamboree. For instance, members of the DIYbio community[159] were found wandering about MIT's hallways that weekend; this is unsurprising as key founders of DIYbio were originally inspired through their experiences in early iGEM years. DIY biohackers were visible with their T-shirts, sticker give-aways (Figure 6.7, top row) and because some members of this movement have celebrity status in

[159] http://diybio.org/.

synthetic biology circles (owing to extensive media coverage[160] and heavy online presence). In speaking with DIYbio enthusiasts, it was clear that not only did they attend the Jamboree to hear about new amateur projects, but they also had a few messages to deliver:

- Firstly, the organization's mission: DIYbio is a fun sub-culture of synthetic biology enthusiasts who support open and safe endeavours of citizen scientists, amateur biologists and biological engineers.
- Secondly, the organization's position about effectively and responsibly achieving its mission: DIYbio's success requires education for amateurs, access to experts, a code of ethics and leadership that supports bioengineering outside traditional professional settings.
- Thirdly, many wanted to express disappointment at iGEM's closing the doors to DIYbio participants, when it was initially announced that the competition would include teams of amateur biologists.[161]
- Finally, DIYbio wanted to encourage growth of their community and sought to help iGEMers who wanted to join existing DIYbio hubs, or create new ones (they now exist all over the world, with a select few being quite active – Boston, New York and San Francisco).[162]

[160] A small sample of media references to DIYbio: Boustead (2008); Bloom (2009); The Economist (2009); Specter (2009); http://www.youtube.com/watch?v=-IIWH6Hhcnc.
[161] On February 9, 2009, it was published in the DIYbio blog that amateurs would be included in the competition (http://diybio.org/blog/diyigem). On April 10, 2009, it was announced that the offer of DIYers competing was withdrawn (http://diybio.org/blog/igem-closes-doors-to-amateurs).
[162] http://diybio.org/local; http://genspace.org/; http://www.meetup.com/biocurious/.

Figure 6.7: Other affiliated selling points

Top left attributed to iGEM and David Appleyard; top right attributed to DIYbio.org; bottom attributed to James King (James introducing FBI and UN members to 'The Scatalog').

Another keynote group included members of the FBI and the UN, who were attending the Jamboree to relay messages concerning biosecurity. Notably, the FBI is a major iGEM sponsor; it is their belief that these young aspiring synthetic biologists are key people to get their message to. On Saturday evening an informal presentation and Q&A session on biosecurity was held in the same auditorium that only hours earlier played host to the Edinburgh team's presentation on creating microbiological landmine detectors.[163] This biosecurity session was orchestrated by Piers Millet from the Biological Weapons Convention

[163] http://2009.igem.org/Team:Edinburgh.

Implementation Support Unit, of the United Nations Office at Geneva, Switzerland. With Piers were four FBI agents. This session was not particularly structured, with audience participation being the focus after each panellist gave a brief autobiography and described how their work related to "securing synthetic biology". Most panellists had a background in life science but had moved careers into government and national security work (from a couple speeches, it seemed as though the audience was given a story about the excitement of career moves into the FBI). The experts spent a good deal of time discussing with the audience, "Biosecurity: What is it?" After responses that ranged from "it's about bioterrorists" to "it's about creating laws and policies", Piers said plainly, "biosecurity is about responsible research and controlling risks". This positive angle was meant to show that there is a reasonable, responsible and exciting way to progress synthetic biology – which was (and is) obviously the desirable route for almost every audience member there. Still, just how risks could be controlled – or, *to what extent* they could be – beyond continuing to use familiar laboratory safety practices, was a matter of debate, and remains as such in the wider synthetic biology sphere.[164]

Interestingly, these biosecurity experts seemed calculative in trying to portray themselves as supportive and friendly with the emerging synthetic biology community. Moreover, they were conscious of resistant feelings that their cause

[164] Notably, the US Presidential Commission for the Study of Bioethical Issues hosted a series of meetings in 2010 and 2011, and produced an extensive report on the ethics of synthetic biology. The report (US Presidential Commission for the Study of Bioethical Issues 2010) suggests that "safeguards" and continued "monitoring" of synthetic biology safety is necessary, but there is no indication of needing to use precautionary measures that go beyond the standards of microbiological and genetic engineering protocols that have been followed for several years (e.g. the use of "suicide genes" and specific nutritional dependence of microorganisms so they could not survive outside laboratory settings).

comes up against: (i) most lab practitioners feel that they are already heavily-regulated and don't like the idea of adding new hurdles to their research endeavours, and (ii) many make the point that *biological engineering is actually really difficult*, so believe that the worry about bioterrorists doing sophisticated genetic engineering is a bit misplaced (e.g. Wouldn't terrorists prefer to just make a bomb that had a reasonable chance of working?). It was clear then, that these biosecurity experts exercised concerted effort in showing their stance as *pro-synthetic biology progress*. The additional take-home message was merely that everyone needs to work together to ensure that synthetic biology develops with good communication between security experts and practicing synthetic biologists (particularly those who participate in a DIYbio capacity).

One final highlight of this session cannot go unmentioned – it concerns how one of these experts really wanted to sell himself as a *friend* to these young synthetic biologists. 'Hi, I'm Dan and I'm the local FBI guy here in Boston', he proclaimed. His message was that in order to make sure that the FBI didn't get confused or unjustifiably worried about the biotechnology work that audience members may be carrying out (now, or in the future), it would be advisable that DIYbio enthusiast just 'call [Dan] up' and 'let [him] know what you were working on, where and with what intention'. This kind of casual communication, he claimed, might be the key to preventing the FBI from storming into an innocent DIYbio geek's garage laboratory. An amusing caricature was apparent in Dan's short talk: the FBI knows that there are *good guys* and *bad guys* who do biotechnology. According to Dan, it seemed like everyone that he had met in iGEM fell into that good guy category, showing how synthetic biology can do some 'neat stuff';

however, everyone in this field is responsible for ensuring that they could easily be identified as good guys, so that the FBI wouldn't mistake them for bad guys. This may seem overly simplistic, but the scene was truly that amusing.

There were also the designers, Daisy and James, who went to the Jamboree, armed with a briefcase of mocked-up coloured poo, to tell a story about how design could help incite important questions around synthetic biology's potential future with respect to matters of feasibility, safety and ethics. The Scatalog was designed to reflect an imagined future application for the Cambridge team's project – a (hypothetical) cheap, personalized disease monitoring system, consumable in the form of an E. Chromi yoghurt drink that would render a person's faeces different colours that could be charted according to various pathologies (Figure 6.8). Daisy and James explained to me their multiple intentions behind their guerilla style presentation of the Scatalog as they revealed the shocking contents of their suitcase to as many Jamboree attendees as possible:

- *Provocation:* The Scatalog was intentionally designed to be a stark contrast to the mechanical, engineered, standardized and sterile ideals of synthetic biology. Synthetic biology is full of simplified imagery of BioBricks, circuits, bacteria with cog wheel graphics and, for now, its practice remains in laboratories, where it seems contained, visible and measurable as scientific objects and tools. The Scatalog, on the other hand, takes a view of synthetic biology arriving at the human scale in a biomedical application. Furthermore, Daisy and James wanted this application to reside in the parts of the body where *E. coli* bacteria would *naturally* be found – in the digestive tract. The resulting

indicator output – coloured poo – would be sticky, messy, dirty. Showing that a re-introduction of synthetic biology into human biology may not at all be so engineered, mechanical or sterile was key to this project's message.

- *Asking a synthetic biology-literate audience about feasibility and safety:* Daisy and James were keen to hear views from experts and aspiring synthetic biologists on the feasibility and safety of their Scatalog. They received mixed reviews; however, in a given synthetic biology audience, the majority tended to believe this application might be safely possible in the future.
- *Asking about acceptability:* Trying to gauge a sense of the moral and social acceptability of their proposal, Daisy and James wanted to hear observers' opinions on whether or not they would really want this level of self-diagnosis in the future? What kind of society would want such a personalized disease monitoring system? Would it be one with an even more ratcheted-up anxiety and sense of personal responsibility for one's health and wellbeing than we are part of today? Interestingly, presented to a scientific audience, it was almost uniformly desirable to have such control in monitoring one's health; however, at a wider societal scale, it would almost surely be the case that some people would prefer 'not to know'.
- *Asking whether, and how, design and biotechnology may work together meaningfully:* In working with synthetic biology practitioners, Daisy and James were struck by how often the term *design* was used by scientists and engineers dreaming up, and

attempting to build, biological machines. As such, they were keen to understand what a synthetic biology view of design might be, finding many parallels with their own training (particularly in industrial design). However, they also saw opportunities for expanding the synthetic biologists' conception in forming a working relationship with professional designers who tend to ask additional, and different sorts of questions. Synthetic biologists and designers both use design in their work to solve problems, but Daisy and James believe that thinking diverges then into (i) an engineering approach (in synthetic biology) and (ii) a human-scale approach (in classical design). The first approach, Daisy explained, is about "efficiency, minimizing cost, finding a way to do something"; in a designer's approach, solutions are catered around "who we are as people and what we need to live better lives". So, Daisy and James wondered if bringing classical design thinking into synthetic biology may be a more efficient way of giving people what they want, in terms of the products and applications that the field eventually aims to make. The wider results of integrating design perspectives into this field remains to be seen.[165]

- *Help promote the Cambridge team's work:* Though careful to separate the real synthetic biology that the students did on E. Chromi from the design proposal, Daisy and James' presence at the Jamboree with their special briefcase certainly received a great deal of attention. After only a couple of viewings, word of the Scatalog spread wildly at the

[165] The Synthetic Aesthetics project (http://www.syntheticaesthetics.org/) has brought together synthetic biologists, social scientists, artists and designers to explore the potential of these collaborations. We await publications and exhibitions to describe this work.

Jamboree and everyone wanted to see what was in the case! This attention undoubtedly further promoted the Cambridge team's work.

Figure 6.8: Scatalog

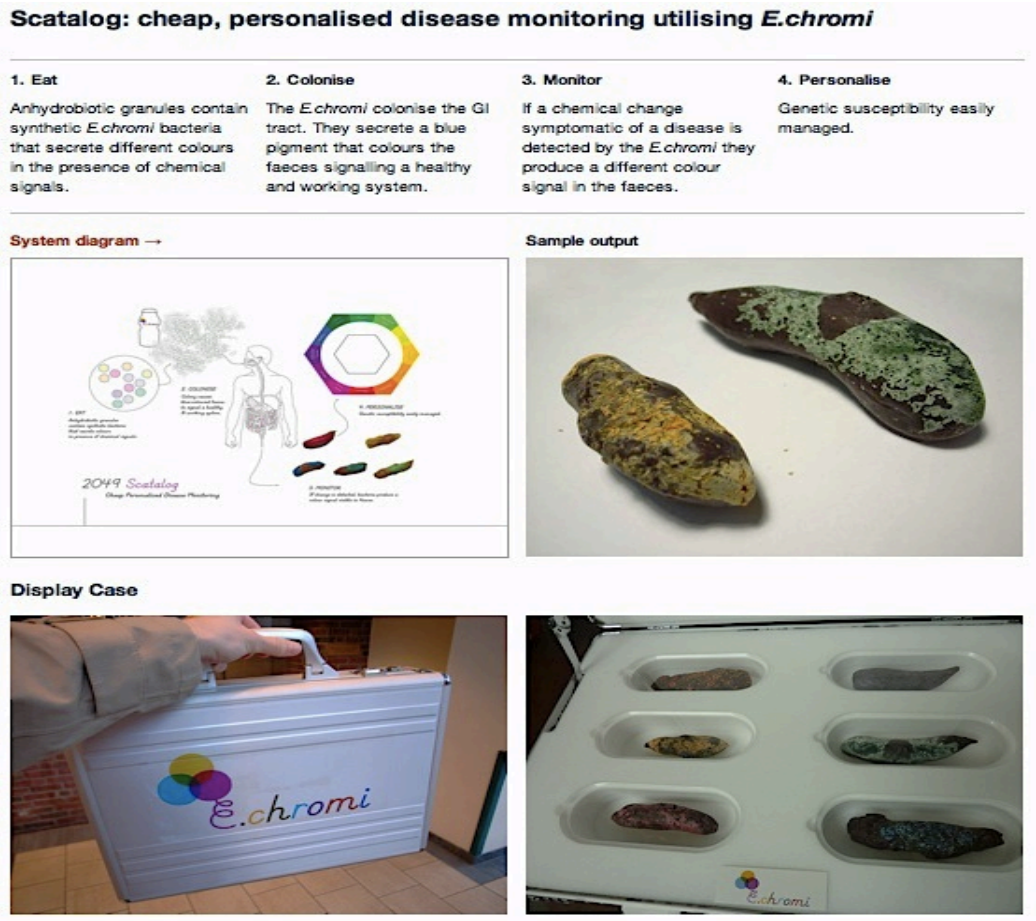


Image credited to Daisy Ginsberg and James King.

Though I will not go into detail, a couple of other stakeholders at the Jamboree are worth mentioning. There was a strong media presence, which included followers from Discovery, Wired Magazine, The New York Times, National Public Radio (NPR) and others.[166] In my view, reporters would have had little difficulty in turning this fascinating network of ideas, extroverted characters and possible

[166] Bland 2009; Ginsberg 2009; Mooalem 2010; http://www.sciencefriday.com/program/archives/200911063.

futures into stories for a public audience. Biotech and pharmaceutical companies were players on scene, there to sell their companies' services, tools and technologies, but also to recruit interest from iGEMers in joining their workforce. These biotech representatives had the somewhat awkward position of being seen as 'the dark side' in the views of some extreme open source enthusiasts; still, there were plenty of iGEMers and advisors who were keen to explore potentially lucrative, private sector opportunities. It is key that the reader has gathered a picture of the iGEM Jamboree as a kind of showroom, brimming with excited community spirit, fascinating projects, story telling, recruitment and hyperbolic messages of various sorts – all on display and convincingly sold and resold, in the over-arching belief that synthetic biology is *the* exciting, new, sexy biotechnology that is full of potential.

Conclusion

This chapter has shown how the Jamboree context – with its dramatic location, exciting attendee list, impressive presentation schedule and larger-than-life parties – created an ideal atmosphere to entice appreciation for synthetic biology projects and broader philosophies. Students gave selling performances of their works, delivered to a keen audience. iGEM leaders presented back to attendees a set of community ideals (in speeches, as well as closer interactions with teams) about embracing creative curiosity, making a difference, openly sharing knowledge and materials, and enjoying the benefits of a new field with a prosperous and exciting future. Other groups too – such as DIYbio, the FBI and designers – took the Jamboree as a place to stage their positions about synthetic biology. The next chapter segues into judgements that were made following these sales pitches, and

the subsequent decisions of iGEMers (as well as advisors and institutions) to join the synthetic biology club, or not.

7. TO JOIN THE CLUB, OR NOT

As the Jamboree weekend neared its close, involved participants were making a number of judgements. These evaluations change over time and are sometimes wavering; nonetheless, I argue that they significantly influence who *joins the synthetic biology club, or not*. More strongly, an investigation of these judgements shows how iGEM has been an effective tool through which to grow and socially and culturally engineer an international synthetic biology community.

This chapter's first section notes which projects were deemed of winning quality. More interestingly, I explore the politics of judging that reveal disparate views on what counts as good synthetic biology. How students evaluated themselves, their peers, the competition and the broader field during, or very shortly following, the Jamboree is examined. Other assessments on the DIYbio community's work, the FBI's presence, the introduction of art and design, and from media perspectives are highlighted too. In 7.2, I describe follow-up sentiments and stories that are more distant from the immediate excitement of the Jamboree experience. At this stage, one can gain a more accurate picture of iGEM's influence in spreading and developing synthetic biology. I conclude by summarizing how I view iGEM as a tool of social engineering, and also by highlighting some recent arguments open to investigation. I suggest that there are significant breaking points that look to be changing the landscape of iGEM and synthetic biology from 2011 onwards; in order to keep pace with this field's state of flux, I suggest that such avenues are worthy of future research.

7.1 Judging ideas

I begin considering a network of judgments that are among the final outcomes of an iGEM cycle with the obvious: as this is a *competition*, there were *winners* (but *no losers in iGEM*) and ways of deciding who deserved such titles. With all Jamboree participants crammed into MIT's largest auditorium, out of over a hundred teams, six finalists were announced on that final Monday morning: Cambridge, Freiburg bioware, Groningen, Heidelberg, Imperial College London and Valencia. These groups presented their works again in order to contend for the Grand Prize BioBrick trophy. For the Cambridge and Imperial College lot, walking into MIT's largest auditorium and seeing their team on that final list marked the beginning of a very exciting end to their iGEM experience; for other hopeful teams that didn't make the cut, that was a moment of sinking disappointment. I won't detail presentations and their selling points again (though, thankfully, Imperial College presenters toned things down a notch in the second round) and shall skip to the awards results. In keeping with iGEM's community spirit that (almost) everyone is prize-worthy, the competition grants virtual Bronze, Silver and Gold medals to teams that satisfy certain criteria[167]. These basic medals were announced first, projected on screen and loud cheering ensued. Then, the special prize announcements began: Best New BioBrick Part, Natural (ULB-Brussels); Best New BioBrick Part or Device, Engineered (EPF-Lausanne and Freiburg Bioware tied); *Best Human Practices Advance (Imperial College London and Paris tied)*; Best Model (BCCS-Bristol); Best Experimental Measurement (Valencia); Best New Standard (Heidelberg); Best Wiki (Heidelberg); Best Poster (Freiburg bioware); Best Presentation

[167] http://2009.igem.org/Judging/Judging_Criteria.

(ArtScienceBangalore). Track winner announcements followed: Best Food or Energy Project (UNIPV-Pavia); *Best Environmental Project (Cambridge)*; Best Health or Medicine Project (Stanford); *Best Manufacturing Project (Imperial College London)*; Best New Application Area (Valencia); Best Foundational Advance (Alberta); Best Information Processing Project (TUDelft); Best Software Tool (Berkeley Software and Illinois-Tools tied). There was, of course, copious amounts of clapping, whooping, screaming and jumping around throughout the ceremony, with every winning team getting up on stage, receiving a trophy, shaking hands with synthetic biology celebrities and smiling brightly for the cameras. This lasted about an hour until the ascending order of prize-winning importance reached its climax and team Cambridge was declared overall competition winners. Images in Figure 7.1 (and the second photo in Figure 6.6) illustrate this ceremonial scene.

Figure 7.1: And the winners are…

Photos attributed to iGEM and David Appleyard.

More intriguing than who won what, are the politics behind judging iGEM. It turns out that there exist many differing opinions about what counts as important in this contest and in synthetic biology, technically and culturally. One prominent disagreement circulates around the value in rewarding big ideas that align with the 'how synthetic biology can save the world' spirit; such projects, though exciting and inspiring, rarely amount to substantial, functional contributions. On the other hand, there is the possible choice to reward more modest projects that can, at their best, actually contribute valuable tools, parts and insights for synthetic biology practice. I have discussed this subject already, and have noted a clear difference in the Imperial College and Cambridge approaches, but some additional interview clips help flesh out this contention:

> What I've seen that's interesting is to start with a blank slate challenge to students, but then take that a step further by reminding them that they live in a world that has problems, challenges, opportunities – and, has engineers.... One of their first responsibilities, in fact, their first responsibility – which is often skipped over in the engineering educational process – is to choose what to work on and a lot of engineers just sort of, 'oh, somebody hired me to do this so I'll do it'. But that's not really what the world needs; the world needs engineers who can look outside of where they are and take some stock of the state of things and help. – Assistant Professor Drew Endy

> I think the synthetic biology community is celebrating things that are… imaginative and new, right. I don't think it's the only aspect, because I think there's also a celebration of things that are *useful*… If you look at the Heidelberg team this year (2009), some people were complaining that they didn't think it was that creative or imaginative – you know, people have done promoter engineering before. I loved it. Because I saw it and was like, I can use that stuff! And we were just talking about how we needed that in the lab. And so to see someone go through and do what I thought was a really good job, I was totally jazzed because I just thought someone did a really great job of building a library that I feel comfortable using.
> – Professor Christina Smolke

> One of the points about iGEM is that it is a competition and it is very media driven so you have to go for the flashiest application you can think of. And that, in my opinion, leads to bad science and bad technology. And there is a lot at iGEM that, in my opinion, I wouldn't trust – just pure waffle. But, it also means we have to go for an application that is high profile, otherwise we won't be seriously considered. – Pierre, Imperial College iGEM advisor

In speaking with judges and having observed a couple of their insider meetings, it was apparent that there were many further disagreements regarding what was significant to synthetic biology. Some were insistent about a strict following of the BioBricks-based approach, firmly believing that the best way forward is to have a library of standard, highly characterized components because this is the optimal way to utilize an *engineering cycle*. Others revealed their position that though they'd like to design and build functional biological systems, synthetic biology is not yet sufficiently advanced to exclude approaches that do not conform to the engineering and accumulation of BioBricks, as pushed in iGEM. Such advocates generally believe that this field should simply help researchers develop tools to do the work they're pursuing; moreover, they take the position that it is currently not helpful to delimit, or even to really define, what is and is not synthetic biology. Taking that line of argument, some professionals believe that this 'new' area really just folds into and extends other fields, such as

metabolic engineering, or plant genetics, for example. Of course, it is important to point out that this sentiment is usually reserved for candid conversations, as most people in this community see the merits of claiming synthetic biology's 'newness' in order to finance their research pursuits.

Another interesting view from judges that arose several times was that iGEM projects are often blinded by their framework – they set out to solve a problem with biology when there is already a non-biological solution, or when there is obviously a better means and method to tackle the problem than with complex living material. According to Drew Endy, "an important thing that I think is missing from a lot of projects is to ask the team to consider alternative approaches that are not based on biology – so competitive analysis of other ways to solve a problem". Spelling this out further, Frederick from Cambridge remarked,

> Many iGEM projects … either address solved problems or the wrong problems in the real world. So, for instance, Imperial's protection of bugs from the stomach – there are a lot of drugs on the market today that have to be protected against the stomach and they have enteric coatings already. That's a completely solved problem!

Judging politics goes beyond disagreeing over the qualities of iGEM projects in terms of their approaches (BioBricks or not) and overall visions (grand or realistic; targeting an unsolved or solved problem). Roger felt, for instance, that the international nature of the competition was enormously important and "the fact that they had six European teams as finalists was a very poor decision – that was wrong". He continued,

> If you want to have the whole world engaged in this, then you've got to have the United Nations. You know, it ain't going to work if you don't have an Asian team or an American team at the final… You

> want to encourage these kids – there should be two teams from each continent...

To me, this commentary exemplifies a wider sentiment that sees the competition as having an important role as the media friendly image of synthetic biology. Interestingly, at highly professional meetings, conferences and policy-related symposia – especially when audiences include social scientists, reporters and politicians – speakers often call attention to the exciting and educational nature of iGEM and how it has infectiously led to the field's international spread. Some view this *happy face of synthetic biology* as an especially valuable contrast to the field's *serious* challenges around biosecurity, economic and legal dilemmas.

Also related to presenting a certain sense of this field as virtuous, I found different opinions as to the value of integrating human practices in the competition (discussed further in later sections). Christina Smolke, official meta-judge of 2009, told me that human practices judges were disappointed by the superficial nature of students' efforts in this area – most teams were just ticking another box. I saw this first-hand in my experience with the Imperial College team, throughout the competition and in conversations with human practices judges. Yet, there were a small number of genuinely impressive efforts in this area and it is clearly valued as representing the competition's open and responsible ethos.

Christina Smolke and Drew Endy both explained an experimental approach to iGEM pursuits (and synthetic biology): an idea exists, a group of people try to take it forward in some way, mistakes are made, lessons are learned and experimental cycles move forward, hopefully making improvements. This was how the competition developed as a whole since 2004, and it is how the

integration of human practices has been working (since it began in 2008). Endy believes that at the end of every iGEM year, it is the judging panel's responsibility to "diagnose what's been experienced so far… celebrate what's surprisingly, unbelievably impressive… which means it's probably worth doing again and again and again, and then figure out how to do it better". That positive perspective is, however, actually mixed with several frustrations between *scientists and engineers* in one grouping and *human practices people* (generally coming from science and technology studies, sociology, philosophy and theology backgrounds) in another.

Fairness in iGEM is certainly striven for – seen, for instance, in the added layer of meta-judging reflexivity – but it will always remain, to an extent, problematic. I have already shown that there are biases in judging what qualifies as good synthetic biology; there are views about keeping up iGEM's international, media-friendly nature in a way that must be crafted beyond the merits of students' work; there are hierarchies that operate across differing kinds of judges (those with technical expertise being prioritized over human practices); and, it is simply impossible to educate and provide fair resources for over a thousand students, all coming from very different educational institutions, with diverse expertise, levels of help, funding, talent, equipment, sponsorship, etc.

I shift now to how students judged themselves, their peers and, most of all, the merits of synthetic biology's community and philosophies. While at the Jamboree, among synthetic biology stars offering personal congratulations, prizes, media attention and a general frenzied atmosphere, many students (particularly on

successful teams) were sold on synthetic biology, wanting nothing more than to join the club and continue on with a prosperous and morally motivated career in this field (e.g. as suggested by Randy Rettburg in the closing ceremony, p. 225). A great number of students were of course, on the other side of that coin, as they left the competition without prizes or attention, feeling defeated and depleted, after all their weeks of hard work. There were also students who, despite not taking home prizes and glory, remained inspired. The Jamboree's uplifting quality and the chance for students to interact with so many interesting projects and people served as enough reward for many to want to continue synthetic biology pursuits.

This comment from Senni reflects a delighted surprise (uniform among the Cambridge team's students) about winning the competition; it also shows how his previously hesitant views around the hype of synthetic biology were altered by the Jamboree experience.

> The fact that we won – *I can't believe it!* The fact that *we* can win is a good sign for the field – you can do simple but good projects and do well. I think that is more important than, like some teams, where their entire university is helping them! I see a bigger world of synthetic biology now – there are actually people out there who believe in this thing. I think there are things going on. It does have a future. Previously, I thought not really – maybe after fifty years… But now I think it will come sooner.

Teammate Derek expressed similar surprise: he thought iGEM and synthetic biology were about celebrating really ambitious projects, ones with "800-odd BioBricks" or "the fact that another team had two patent applications" (not that this was celebrated in iGEM but that it reflects high ambition), and so he was quite amazed that their project was so well received. In the immediate aftermath of the Jamboree, the fact that the Cambridge team's work – self-reflexively

considered as exciting yet modest, simple and realistic – championed iGEM 2009 gave the students considerable hope in the future of synthetic biology.

Some of the Imperial College students' reflections, shortly after the Jamboree, are captured in the following excerpts. They are further evidence that, as Zach so poignantly remarked, "iGEM is the process by which this school of thought is indoctrinated into you, from the ground up"[168]:

> The experience at MIT was amazing, firstly. When you're working in a field that's more developed, you wouldn't actually get to meet the leaders in one summer. And to go to MIT and to have Randy Rettburg, Drew Endy, Tom Knight, … everyone there! That just goes to show how tight this field is… It is this neat little community. That hit home, going there. And everyone is interested in everyone's work. Even though we're iGEM students, the leaders of the field are there and they want to come to our talks and talk to us about the kind of stuff that we're doing. And that just shows that we're learning from them but they are also learning from us – there is a lot of bouncing ideas around. That was really cool. – Sita

> I think iGEM is one of the big facilitators of *synthetic biology as opposed to genetic engineering* in as much as genetic engineering was kind of stalled by campaigners against genetically modified organisms. But in synthetic biology, if we could redesign the whole system in the most efficient and most controlled manner – this modular way. It's kind of like the most efficient language that was ever invented… What was it called? Esperanto. – Zach

[168] In additional team interviews, I found similar expressions of being sold on synthetic biology:

- UCSF student A: "I think iGEM is awesome. It is my first time here. We have a few veterans who are coming back for the second time but for our first time, we came here and thought, 'we don't know what to expect'. Then, our first day here, we checked out some presentations and a lot of us were surprised with the new ideas, new applications coming in and just putting it out there for everyone to view. And, it's also good because it is in different areas – not only focused in one area."
- UCSF student B: "For me, I feel a lot of pride in being part of this pioneering new, young field. There are lots of people in my college who don't even know what synthetic biology is. But, in ten or twenty years from now, synthetic biology is probably going to be the first thing they'd think about when they think about biology or some scientific field that they'd want to get into."
- UCSF student C: "A lot of the ideas here, if you are working in a real lab, they wouldn't let you do all these crazy ideas that might actually turn out to be good ideas. So this is the place to test those ideas"
- Valencia student A: "I knew synthetic biology through iGEM; I didn't know it before. I recommend it to everyone – it is fun, it is instructive, and you meet a lot of people."

> I think iGEM is really great in that it shows how exciting this field really is. I never knew before what this was all about. And so it is just a really great route into the field. And with some of the projects, you get just some really great ideas coming out of it. The creativity there is really quite amazing. Some of the ideas are quite, I dunno, headline grabbing, I guess. Which is good for the field if you get people interested. – Matt

However, not everyone was sold on synthetic biology's popular narrative. Kajan departs from the views above:

> I think iGEM is a good springboard for this kind of thing but I don't think it is a very sustainable way for the field to develop… So, after iGEM, centres have to develop and go forward… I think, after a period of time, when the field gets sufficiently developed, I think iGEM can stop and the research centres themselves can go on to do more substantial research.

This point will be discussed again later in this chapter when I explore breakages from iGEM.

Following their human practices award win, I asked some Imperial College students to turn this judgment back on themselves, to reflect about the process in this aspect of their project. Candidly, there were admissions of surprise and expressions of gratitude, as it was recognized as mainly the work of Charles and myself. The team was nonetheless happy to have the prize. When I spoke with the students over coffee after having arrived back in London, Sita recalled speaking to a human practices judge who told her that they were tired of the same old leaflets and questionnaires; what struck the judges about Imperial College's work was that the team implemented their considerations of human fears in their actual design by including the genome deletion module. However, Zach jumped in correctively:

> I would agree that that was the reason we won but I don't think we deserved it for that reason because the idea of genome deletion came up very early for different reasons. It was originally that we were trying to delete the plasmid because people don't want to have that

> inside them… It wasn't like there was a big debate. It was just obvious. Nobody needs some kind of extra intuition to understand that. And the other thing, of course, was dosage control. Those were the two big things that factored into doing genome deletion. It wasn't that we'd re-designed it – but that was the line that we sought because it is a competition.

The students' comprehension of their own spin on the human practices process was evident.

Further in this conversation on human practices at iGEM, some students expressed that the emphasis on doing this kind of work alongside the already demanding science labour creates another unfair bias in the competition, working against teams that do less controversial projects. Students who are new to the social sciences intersections with biotechnology often don't know what this kind of work could involve and, lacking help and support, many teams resort to doing surveys and outreach, asking others' views on synthetic biology's social and ethical consequences as they don't yet feel they've got their own opinions on such matters. Now that human practices has become increasingly important (albeit lesser to the technical evaluation of projects) in the iGEM judging circle, asking teams to go beyond surveys in order to be recognized in this category is unfair, claimed a couple of students. Yet, another student's opinion resounded positively:

> I thought the human practices exercise was really quite interesting and it opened up my eyes to different issues that are sort of more important in the field. And I think as far as synthetic biology goes, it is really quite relevant to talk about these things – it is important for how the development goes… And, as a lot of us are planning to go into the field, I think it is useful – quite important that, at this stage, we explore these things.

This group discussion with Imperial College students may have revealed a mixed view of the importance of human practices; however, the conversation's conclusion was particularly interesting:

> **Matt:** I think also having won the Human Practice prize must have been great for you [directed at me] and it must have done a lot of good for the relationship between Imperial and the BIOS Centre. You've changed people's minds about this.
>
> **Zach:** Bernard has come around…
>
> **Matt:** Yeah, he was really closed minded about this stuff before… And I think, from that perspective, it is really great what you've done.
>
> **Caitlin:** Well, I hope that it has sparked some lessons learned…
>
> **Sita:** Yeah, I think that's a good thing.

I will highlight the theme of how a social science intersection in synthetic biology is viewed and to what extent it is valued later in this chapter and in the next. It is indeed fascinating to have witnessed (in retrospect) what assisting with a human practices project revealed over time: it began with resistance and side-lining until the project was contained and mainly worked on by myself and one other student; to my surprise, the team won a prize through spinning sales tactics; and, further to my amazement, there seemed to be some partial redemption in a few people's reformed beliefs that this kind of collaboration between social sciences and practicing synthetic biologists really deserves more attention and credit.

Let us move away from how students judged the merits of synthetic biology as well as their team's own Jamboree performance to another set of ideologies on sale at the Jamboree, those of the DIYbio community. In several informal discussions, I gathered a mixed body of feeling, support for and clear attitudes against DIYbio. On the one hand, many expressed great positivity about making biotechnology popular and accessible, and certainly the DIYbio spokespeople do a good job in

getting attention and drawing interest. On the other hand, even resounding cheerleaders of iGEM and an open source ethos could be sceptical, feeling that this fringe group of garage biohackers go one step too far and risk giving synthetic biology a bad reputation. That is, some believe DIYbio is a potential threat-by-association to the well-intentioned practice of synthetic biology in *proper*, established laboratories that abide to tedious but necessary systems of health, safety and security regulations.

A few additional (and dramatic) sentiments against the DIYbio community, voiced by Claire (a synthetic biology PhD student at Harvard), are noteworthy:

> [A prominent DIYbio advocate] was trying to tell me that he was going to be more innovative than I could ever be because he has to work around the constraint of not being funded. But, you know innovation means different things. I am sure he is going to make a fabulous gel box, but…. If you can talk those outspoken, self-righteous DIYbio people down a little and actually get them to talk about the biology – like what are they doing that is not just hype?! I mean, they're not doing synthetic biology – it is outrageous for them to even suggest that they are. I mean, *it is hard to do*! There is a lot of stuff that you need first of all! It is good in terms of getting people into biology, but really – what is extracting DNA from a strawberry going to do?

Claire continued to inform me about how basic the work was from DIYbio practitioners and though she supports their popularization of science whole-heartedly, she finds the rhetoric of their mission rather difficult to bear. In spite of the length of the following excerpts, I hope the reader appreciates the frank expressions of opinion:

> The language that they use is about 'we are going to make a biotech company in our garage…' And the idea that DIYers are going to develop synbio in a way that mirrors electronics! That is just not realistic – biology is not computers!
>
> And they also use a lot of language of oppression – as if we have some sort of natural right to do science and that there is some sort of

> institution that is 'repressing them by not letting them do science'! These are white guys with college degrees – no one is stopping them from doing science! They could get a job, in a lab, doing science – tomorrow! I mean on the DIY website, there have been recent discussions about, you know, 'if there are laws against you, you have to fight against them – like Rosa Parks and Ghandi!' This is ridiculous, this notion that there are 'unjust laws that are preventing DIYers from doing science'! I find it offensive to bring up the Civil Rights movement to talk about a bunch of 20-something white guys doing science! It is actually offensive! And, they could do so much good because it is kind of hip and they are cool guys who love science – they could do so much good with that.
>
> You know, DIYers criticize scientists for being so isolated and that academic scientists are pushing DIYers away. But, part of what I want to do is explain my science and try and reach out. And then the DIY attitude towards other scientists is sometimes aggressive. I mean, yes, I work at Harvard but I am not trying to be mean or oppress DIY scientists. It is also interesting from a labour point of view – I mean, I do this to make a living. I get paid to do my science. I understand hobbies and investing money in those hobbies – but, to do science and put money into it, *as a hobby?!* That is a bit crazy!

Clearly, there are numerous points of divergence between Claire's academic perspective and her view of the DIYbio culture – on everything from what is possible or innovative in biological engineering (given that *it is hard to do!*) to the moral authority of citizen scientists resisting established institutional norms. Though much further discussion on this topic is warranted, it is beyond the scope of this work; the important point is that this kind of judgement exists in a sea of evaluations, and that the Jamboree creates a perfect storm for several positions on various aspects of synthetic biology to come together.

Another point of consideration is whether or not Jamboree participants were interested in, or taking seriously, messages about securing synthetic biology. In the last chapter, there was something quite odd about a local FBI agent taking stage to convince iGEMers about the importance of open communication so that security experts could have a clear picture of good guys and potential bad guys in

synthetic biology. There was awkwardness about the FBI presence at iGEM – although every suggestion was made that the organisation supports having fun and learning by engineering biology and the representatives concertedly displayed an up-beat attitude, it was nonetheless strange to have official government agents walking around an undergraduate science competition with guns in their belts.

A number of people I spoke with expressed appreciation that a connection to biosecurity experts is necessary and they take seriously the idea of a community responsibility to develop a code of ethics that ensures safe and secure practice of genetic engineering. Certainly American practitioners of synthetic biology and members of the DIYbio community see links to the FBI as compulsory. Others – especially those from countries that are less acutely concerned with terrorism than in the US – are sceptical of the need to get so excited about bioterrorists when it is actually extremely difficult to execute synthetic biology reliably. They might typically raise the question of why anyone would want to use this technology to make weapons when there are many easier technologies to utilise in order to achieve those ends. Such views often think the biosecurity concern is rather misplaced in synthetic biology at this time. Other participants had very little idea about biosecurity or international politics and seemed uninterested in this subject's tie to their practice. These are often people who express a desire to just get on with their work and though they will obey the rules, they dislike the idea of further restrictions in their scientific endeavours. As biosecurity authorities have declared that they do not intend to restrict good bioengineering that aims to make the world better, some synthetic biology practitioners just hope to stay out of complexities in developing connections with FBI agents.

Despite a range of judgements about the biosecurity presence within synthetic biology communities – marked mostly by a certain ambivalence among Jamboree attendees (as one can easily imagine it is bizarre to know that your work, as an undergraduate student, is tracked by a top national intelligence service) – this relationship will remain and biosecurity experts show signs of deepening their connection and infiltration. In 2010, a security presence at the Jamboree was apparently stronger, and a thorough website has been included among the iGEM pages as an awareness-building and educational tool for students.[169]

The integration of art and design perspectives has been embraced and become influential in the community since its beginnings in 2009. At a local level, involving design viewpoints from Daisy and James in the Cambridge team's project was regarded as an absolute success by all participants in its inspiring new and fun ways of thinking about both this particular work and the wider field. When Daisy and James brought their Scatalog of coloured poo to the Jamboree and displayed it guerrilla-style, a great deal of intrigue was generated – seemingly every attendee wanted to peek inside the case to see the shocking contents that made visible an imagined future application for personalised medicine via synthetic biology. The reactions that this interactive design work received were mixed that weekend, ranging from disgusted faces to giggles, to a good number of people expressing genuine curiosity about how to make such an idea a reality. Other artistic explorations of synthetic biology – such as ArtScience Bangalore's

[169] http://2010.igem.org/Security.

smell of rain project (winner of Best Presentation) and team Osaka's beautiful fluorescent *E. coli* – were highly celebrated at the Jamboree too.

What is most remarkable, however, is the ricochet effect that ensued after the 2009 Jamboree when art and design ventured into several collaborative explorations of synthetic biology – and received a great deal of attention in the process. The following shortlist briefly describes some of the projects, exhibitions and keynote publications in this vein since 2009:

- ***E. Chromi*** continued to live on in Daisy and James' design imaginations. They made a short film, several material objects (illustrating other imagined futures), developed the *E. Chromi* story on the project's own website as well as through a Twitter feed and exhibited their work around the world.[170]
- **Synthetic Aesthetics** (Stanford University and University of Edinburgh collaboration, 2009 - 2011) – An Engineering and Physical Sciences Research Council (EPSRC) and US National Science Foundation (NSF) jointly-funded project[171] that brings together synthetic biologists, artists, designers and social scientists to explore the value of such collaborations.[172]
- **Wellcome Trust windows display *What if…?*** (London, UK, February 1 - July 20, 2010) – Huge window displays at Wellcome

[170] http://www.echromi.com/.
[171] One of five successfully funded projects that were part of a 'sandpit' meeting in 2009 that awarded £6 million to various competing ideas in the area of synthetic biology (http://www.epsrc.ac.uk/newsevents/news/2009/Pages/syntheticbiologysandpit.aspx).
[172] http://www.syntheticaesthetics.org/.

Trust headquarters showed speculative future design projects related to biotechnology, including *The Synthetic Kingdom* and *E. Chromi*.[173]

- **Guerilla Science** exhibits *E. Chromi* at Secret Garden Party, (Cambridgeshire, UK, July 22 - 25, 2010).
- ***Impact!*** (Royal College of Art (RCA), London, UK, 2010) – UK designers and scientific research groups fused in this EPSRC and RCA collaboration. James King's *Cellularity* was exhibited among sixteen other works.[174]
- ***Alter Nature*** (House for contemporary art, Brussels, Belgium, November 21, 2010 - March 13, 2011) – A show of twenty international artists and designers whose works focus on the ways in which human beings change and design nature. James King's *Cellularity* was included in this exhibit.[175]
- ***Nano Supermarket*** **by Next Nature** (Dutch Design Week, Einhoven, Netherlands, October 2010) – Speculative design projects around nanotechnology exhibited; *E. Chromi* was included.[176]
- ***Becoming Trans-Natural*** (Trouw, Amsterdam, Netherlands, March 4 - April 1, 2011) – Daisy Ginsberg and Sascha Pohflepp's *Growth Assembly* work was displayed at this speculative design exhibit.[177]
- ***Brit Insurance Designs of the Year*** (Design Museum, London, UK February 16 - August 2011) – *E. Chromi* was nominated for this prestigious award and an expanded exhibition was displayed.[178]

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[173] http://www.wellcome.ac.uk/News/Media-office/Press-releases/2010/WTX058379.htm.
[174] http://www.epsrc.ac.uk/SiteCollectionDocuments/events/impact-exhibition.pdf.
[175] http://www.z33.be/en/projects/alter-nature-we-can.
[176] http://www.nextnature.net/events/nano-supermarket/.
[177] http://multiplexart.ning.com/page/expositie-tn-02.
[178] http://www.londondesignfestival.com/blog/e-chromi-embedding-design-scientific-research.

- ***Life 2.0*** (Science Exchange, Royal Institute Australia, April 25 - July 8, 2011) – This exhibit considers changing ideas about nature and technology, given synthetic biology's proposal to rebuild life from bottom-up; *E. Chromi is included*.[179]
- ***Talk To Me*** (MoMA, NYC, US, July 24 - November 7, 2011) – An upcoming exhibit on communication between people and objects; *E. Chromi will be included*.[180]
- Ginsberg, A.D. (November 9, 2009) 'Building New Life Forms at the iGEM Jamboree', ***Wired.co.uk***, UK.
- Bleicher, A. (December 11, 2009) 'Technicolor doo-doo', ***The Scientist***, US.
- Antonelli, P. (October 2010) 'Fresh as a Daisy', Feature on Biomedical Art, ***Nature Medicine***, 16:942.
- Neuhaus, L. (January 28, 2011) 'How to humanize technology – from the scatological to the sublime', ***Scientific American***, US.
- Nakajima, K. (May 2011) 'Design in Synthetic Biology', ***Axis Design Magazine***, Japan.
- In the Italian edition of ***Rolling Stone***, a special feature on the world's hot list of design talent includes Daisy Ginsberg in the top twenty (Rawsthorn 2010).

This list's impressive length, notable exhibition locations and media appearances speak volumes of how art and design have effectively staked a place as part of the emerging global synthetic biology community.

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[179] http://www.riaus.org.au/events/2011/04/07/life_20_artifice_to_synthesis.jsp.
[180] *Talk To Me* show yet to go up at MoMA (http://wp.moma.org/talk_to_me/). An interview with James King has already featured on the MoMA blog (May 17 2010): http://wp.moma.org/talk_to_me/2010/05/meeting-with-designer-james-king/.

Following documentary film-makers Sam and George and what they did after their impressions of the 2009 Jamboree was interesting. These two spent over a year driving around the US, interviewing keynote figures in the field, iGEM teams and DIYbiologists so they could tell a real story about synthetic biology – what today's reality is and what tomorrow's possibilities may bring. In the process, they've documented several interesting people and narratives and gathered financial support of over $31,000 (USD) that is currently enabling them to produce their film. Sam and George are hoping to enter their 'Synthetic Bio Documentary' into the Sundance Film Festival. From the beautiful work that I've seen so far, I can imagine this will turn out to be quite an interesting independent film.[181] I will not go into detail about all media presences; reports from the New York Times Magazine, Science Friday (on National Public Radio), Discovery, Wired and many more followed tales of the 2009 Jamboree.

It is certainly remarkable how the endeavours of iGEM students, DIYbio enthusiasts and synthetic biology pioneers have attracted a flurry of additional creative interest – from artists and designers, documentary film-makers, journalists and social scientists – all coming to judge that there are several narratives within this diverse community worth telling. During the colourful excitement of the Jamboree – *the Olympics of amateur genetic engineering* – evaluating ideas and philosophies was on the minds of all participants, both within the sphere of practicing synthetic biologists, or those aspiring to be, and among interested parties on the fringes. In the rather overwhelming three days, almost

[181] http://www.fieldtest.us/bio/about/; http://www.fieldtest.us/bio/videos/.

everyone found an attraction to interesting facets of synthetic biology – people wanted to join the club. However, with reflection and distance from the Jamboree, decisions about further pursuits in the field can change and many realise that several notions in synthetic biology's technical and socio-cultural missions are easier discussed than accomplished.

7.2 Follow-up after the dust settled

Before considering some student follow-up from the Cambridge and Imperial College 2009 teams, I will go back in iGEM history to the 2006 MIT team who engineered *E. coli* to produce wintergreen and banana scents during different growth phases.[182] To date, that remains one of the most talked about iGEM projects, notable not only for being a fun, imaginative and successful idea, but also for representing a kind of dream team. It was a dream team because it had four highly ambitious graduate student advisors (along with five undergraduates and an additional graduate advisor) and Tom Knight and Drew Endy as faculty advisors (founders of iGEM) – all of whom went on to become synthetic biology superstars.

The four graduate advisors teamed up with Tom Knight after finishing their PhD's and co-founded Gingko Bioworks[183], a Boston-based company whose mission is to "make biology easy to engineer". Further to this mission, Gingko's website claims "Only when biological engineering is fast and predictable will we fulfil the potential of biological technologies to revolutionize the provision of food, medicine, energy, and materials". Under that umbrella, the company has been

[182] http://parts.mit.edu/wiki/index.php/MIT_2006.
[183] http://ginkgobioworks.com/about.html.

developing a range of projects, from heavily funded work (sharing $6.7 million from the US Department of Energy with collaborators) on electrofuels to developing IP for DNA assembly technology; from a user-friendly BioBrick assembly kit to biomanufacturing protein therapeutics; from strategic consulting to helping the MIT Registry of Standard Biological Parts improve its catalogue design. The Gingko group has even continued to work on their banana-scented bacteria from the 2006 iGEM project, looking to manufacture flavours and fragrances. This company's formation, its slow but steady growth and its recruitment of iGEM student interns[184] (an example to be discussed shortly) is emblematic of how the competition fuels synthetic biology's development.

Moving back to the particular groups of this work's focus, Cambridge University's first iGEM experience (and for the UK) was in 2005. One notable trend that followed was simply an increase in UK academic laboratories paying attention to iGEM and synthetic biology: by 2006, University of Edinburgh and Imperial College joined the competition and by 2010, the UK was represented by nine teams. Another important point about Cambridge's history of iGEM participation is that it began with a team that included Andy as an undergraduate, who went on to pursue a PhD in the field, advise several iGEM teams, orchestrate conferences, recruit more UK interest in this area (from Microsoft Research, for instance) and work for The Registry at MIT. The faculty involved in Cambridge's synthetic biology circle have also constructed a recognized, credited undergraduate course in synthetic biology that has been operating since 2009. This was the crash course that I took (Chapter 3) and it is not only required for the

[184] I recommend viewing the video that encourages prospective Ginkgo employees to be among the "engineers of the future": http://ginkgobioworks.com/careers.html.

University's iGEM students but is also open to other science and engineering undergraduates at Cambridge who do not participate in the competition. Samuel, Geoffrey and Frederick have all explained to me the great challenges in opening up academic disciplines and divisions at such a traditional university, but they have made some strides (in getting funding and PhD students) and continue to fight institutional battles in order to increase synthetic biology's research presence.

As for the 2009 Cambridge team, about a month after the Jamboree, when I conducted follow-up interviews, the excitement remained palpable as students recalled their iGEM experience. Indeed, everyone continued to express their surprise and delight in winning the competition; the additional congratulations received upon returning to Cambridge kept a certain buzz going and the media features of their work were another thing to smile about. Yet, interestingly, even this champion group demonstrated a cautious uptake of synthetic biology's promises. When we discussed casually the possibility of students carrying on in the field, responses were tepid, at best:

- Derek claimed, "I wouldn't want to be involved in synthetic biology for at least another five years. It is just not practical yet… Synthetic biology's parts system will be old news once DNA synthesis becomes automated – that little printer on the desk idea…"
- Alex felt that, intellectually, what interested him in mathematics and modelling was to look at complexity, not the simple two or three gene systems of synthetic biology. He expressed that, "things don't seem to

be improving at a drastic rate" and, at his most supportive, he said "I am keeping it [synthetic biology] as an option, *if it gets better*".

- Eleonore claimed to "see synthetic biology failing" and that the field as a whole neglected her main curiosity – "It is not interested in what the bacteria are actually doing". To Eleonore, synthetic biology wants to build with biology, without actually capturing what is most fascinating about the microbial world.
- Chelsea said, "There isn't enough of what I'm interested in. I do physics. I mean I might be interested in biophysics."
- Emma, the most supportive of synthetic biology, claimed that iGEM made her "a lot more open minded about jumping into something that is a lot more unstructured, with an uncertain future… Even if synthetic biology doesn't work, the people are still fun and they're having a great time – and you really need people like that to build up a science because it is a really difficult thing… I have a lot of respect for the people in this field who are just really going for it. The idea of jumping into that is exciting but it is also really scary because it means taking a lot of responsibility from the very beginning." Emma continued with a modest, but certainly what seemed to be the most excited view on possibly joining the synthetic biology club: "Right now I am just doing biochem and if I get inspired by my biochem project, then that's great. But I already know that I have been massively inspired by iGEM. So it is definitely an open door, which is really exciting…. The fact that I know the people now and that I'm

only going to gain lab experience and lab skills, which will make me a better synthetic biologist, that's pretty exciting."

By February 2011, sentiments and paths of many Cambridge students had shifted:

- Derek was finishing off his biological sciences degree and applying for biotech positions in San Diego, US;
- Tobey was enjoying his third year of engineering, with another year to go, specializing in Information and Computer Engineering, and though he said he was uncertain about where he may end up, he was taking some biology modules and remarked that synthetic biology still appeals;
- After working for several months in Geoffrey's laboratory, continuing to optimize her violacein sequence, Eleonore was applying for PhDs (and, despite her earlier reservations about the field, her top choices were in synthetic biology);
- Chelsea was interviewing for PhDs in physics;
- Senni had taken up a position as a researcher at the Genome Institute of Singapore, but intends to undertake a PhD position in a yet unknown area of biological science;
- Emma was getting excited to embark on a PhD in metabolic and cardiovascular disease research, based at the Institute of Metabolic Science in Cambridge.

So it seemed that after a year and half of distance from the iGEM experience, the Cambridge 2009 team had recruited maybe two (of seven) students into the wider synthetic biology club.

In the Imperial College story, it is again noteworthy that synthetic biology started at this institution with an iGEM team in 2006. After 2007, one of the team members that year (Max, a 2009 advisor) became the institution's first synthetic biology PhD student, continuing with an infector detector system that they had constructed for the competition.[185] In 2008, the trend continued as two iGEM members followed through with Master's degrees and subsequent PhD work in this subject. In terms of setting up other structures to support synthetic biology development at Imperial College, by 2007, there was an undergraduate course. In 2008, an MRes course was added; by 2009, the successful EPSRC grant allowed the formal set up of the Centre for Synthetic Biology and Innovation (CSynBI)[186], which now offers a comprehensive education program in synthetic biology and has a number of new staff leading various research projects.

For the 2009 iGEM team, the follow-up involves three of eight students carrying on in synthetic biology PhD's (Zach, Andrew and Nisha) and, directly following iGEM, there were four students who completed CSynBI's MRes course in Systems and Synthetic Biology (Zach, Felicity, Nisha and Matt). A couple of students diverged to completely different career paths, such as banking; while Soo and Kajan have been contracted to work for a year in Singapore in biotechnology industry jobs, before they plan to pick up again with graduate studies sometime in 2011 or 2012.

[185] http://parts.mit.edu/igem07/index.php/Imperial.
[186] http://www3.imperial.ac.uk/syntheticbiology.

After pursuing an MSc in Bioinformatics and Theoretical Systems Biology at Imperial College, Nisha has ended up in Samuel's lab at the University of Cambridge, focusing her PhD on computer modelling in synthetic biology. Zach completed his MRes in Systems and Synthetic Biology and is now doing a PhD at CSynBI, proudly stating that he hopes to be a biotech leader one day.

Andrew's story begins directly after the 2009 Jamboree as he remained in Boston to embark on a one-year hiatus from his undergraduate degree, getting industry experience at Ginkgo Bioworks. Andrew worked on developing an automated solution for the purification and building of engineered plasmids as well as the subsequent transfection into bacteria. Additionally, he gained competency in using the latest software that seeks to integrate a complex network of a given laboratory's users, equipment, standards, functions, sample management and workflow automation; and, he carried out experiments using a cutting-edge liquid handling robot[187]. Andrew gained highly valuable practice in using some of the best equipment of synthetic biology – moreover, he was responsible for trying to *improve* the implementation of this software and technology, given the complexity still inherent in any experimental reality, in this relatively new biotech start-up company. Andrew was the first intern at Ginkgo and not only did this work turn out to be hugely valuable exposure to a higher level of synthetic biology practice, his time in Boston and traveling the US allowed him to meet a list of major players in this field, spanning academic and industry laboratories as well as the DIYbio community. When I caught up with Andrew a couple of times following his year in America, he was more motivated than ever as he worked

[187] Such robots in action: http://www.youtube.com/watch?v=tTicZnyvPlA&feature=related.

tirelessly in applying to the most prestigious synthetic biology PhD programmes. Unfortunately, he has not received funding and is unable to commence his next step in this field at this time; nonetheless, Andrew will continue to pursue this dream.

The Imperial College 2009 iGEM team effectively recruited at least three (of eight) students, moving towards a professional career in synthetic biology – this rate is fairly high. Even if, at a global scale, the rate of iGEM alumni pursuing the field further is much lower, it remains reasonable to hypothesize that there is a trend of some significance that demonstrates the competition's recruitment of a sub-section of participants to help grow and evolve this nascent biotechnology.

Thus far, it has been a mixed group of aspiring synthetic biologists and the pursuit of other directions in the iGEM alumni that this work has closely followed. For all the students, the iGEM experience was nonetheless one of tremendous learning and personal development. Previous chapters have explored how some students felt that they'd acquired skills at a whole different level than would have been possible to achieve in undergraduate courses or other ready-designed research projects. In the teams' own building of their ideas, designs, experiments and ways of presenting, biological engineering turned into more of an art form than a simple following of recipes. I have also discussed earlier how this intensive collaborative work engaged students to be self-reflexive about their best role in these particular teams – development as leaders, better listeners, efficient deliverers of results, and becoming more able to receive criticism constructively was evident across the board. After the Jamboree, students also reached new levels of presentation skill

in delivering their project sales pitch several times (not only on stage, but also alongside their poster and during other conversational opportunities). The Jamboree's showcasing of several ideas and philosophies across a wide range of stakeholders also helped to open the minds of iGEMers. Undoubtedly, this competition excels in its ability to train, inspire and indoctrinate a huge number of students, a proportion of whom will go on to later synthetic biology pursuits.

Following up with advisors' views, a perfect passage to begin with is this remark by Andy:

> How else are we going to educate the next generation? For me, as an iGEM student turned ambassador turned advisor, I remember coming back from the Jamboree in 2005 and wanting to tell the world – my mother, my best friend, everyone at Cambridge – about synthetic biology...

The point is clear from yet another angle: iGEM is a unique and effective educational tool for students and advisors involved, and it has also successfully enrolled institutional (and with that, financial) support, as well as the next generation of players for synthetic biology. There is uniform agreement among the Cambridge advisors that their teaching in iGEM is one of the most interesting, fun and effective ways to ignite the curiosity of undergraduates about synthetic biology.

> Part of the appeal of iGEM and synthetic biology, is that you can take students out of the world of lectures and codified information and a view that's hemmed into getting down to an atomic description of some living process… But, what's that for? And, in iGEM, you take students out of that kind of environment and put them into something which uses their existing skills, in a better way in fact, and points them outwards so that they can go explore.
> – Samuel, Cambridge advisor, 2009

Having extensively described, over the course of this thesis, alternative forms of brainstorming, group work, creativity and high levels of independence that iGEMers experienced, I shall not go into further detail.

Another important point for the Cambridge advocates of synthetic biology is that "it's a technology for the young", as Geoffrey put it. Moreover, it's a technology that, at Cambridge, has faced considerable resistance from senior, established positions and disciplines, given the highly traditional institutional structures of the university. Andy explained his experience: "No one wanted to listen, senior scientists would tell me that it had all been done before, and when I tried to explain, get them to understand why synthetic biology was different, they just either laughed or turned away". In that conversation, Geoffrey added "They're too wired into doing things in a particular way and they're not open to ideas, and part of that's arrogance too, because they think they know everything, they think they know the way it works". The resistance that Samuel, Frederick, Geoffrey and Andy faced seemed to only strengthen their resolve to continue building synthetic biology at Cambridge. Frederick pointed out, after the 2009 Jamboree, that there was more hope. The Wellcome Trust announced it would provide student stipends for UK iGEM teams[188] and the BBSRC named synthetic biology as a priority funding area[189]. Subsequently, the synthetic biology clan at Cambridge carried on with new grant applications.

[188] http://www.wellcome.ac.uk/Funding/Biomedical-science/Funding-schemes/PhD-funding-and-undergraduate-opportunities/WTX056624.htm; http://www.wellcome.ac.uk/News/Media-office/Press-releases/2010/WTX059006.htm.
[189] http://www.bbsrc.ac.uk/publications/planning/strategy/priority-bioenergy.aspx.

In one meeting, Andy – perhaps overly enthusiastic about the group's success and still deeply moved by the Jamboree spirit – claimed that the flourishing of synthetic biology was inevitable:

> Synthetic biology has gained momentum and turned from a snowflake into a snowfall into potentially an avalanche. It really is now showing off science and technology and engineering that is not just cutting edge but like, bleeding edge – it's better than anything else that the current techniques, or established traditional techniques can offer, and senior scientists have no choice but to listen now. It's not like they can say, 'Oh we've been doing this for thirty years'. They haven't, because if they had, then where are their data sheets, where are their characterized parts, where are their off-the-shelf components that snap together from lab to lab? They aren't there, and they're not engineers – they're scientists.

This almost outrageous statement indicates a kind of wild hope that being involved in the synthetic biology community can inspire; however, it is crucial to remind the reader that, at another moment – perhaps after a common experience involving weeks of tedious failing experiments – one would find a completely different tone. In its currently early stage, this field is highly characterized by an oscillation between easily talked about grand ideas and difficult realities of practice. In this chapter's conclusion though, I suggest that there are some ideological bubbles being burst and, as a result, many synthetic biologists are trying to find a more constructive middle ground for thought and experiment.

At Imperial College, iGEM leaders similarly echoed that iGEM is mainly about training, thinking and education, along with "getting kids excited about synthetic biology" (Roger). Specific to this institution, for a few years, their synthetic biology capacity was mainly in iGEM but since 2009, iGEM is only one component of the greater synthetic biology network of CSynBI. As mentioned, iGEM feeds into the MRes program, which in turn feeds into PhD research and

helps to fill out the laboratories of new researchers who started at the Centre in 2010. Max told me "iGEM projects sell well" and this, in no small way, was what generated publicity and institutional attention to encourage funding bigger synthetic biology endeavours at Imperial College. Not only has iGEM helped to seed CSynBI, it has also brought people to the Centre from all corners of the globe as many current collaborators began as iGEM-mediated contacts.

Outside the UK, coming from laboratories and universities with greater synthetic biology status and funding than either Cambridge or Imperial College, it is interesting to consider the views of Drew Endy and Christina Smolke, whose work has collectively influenced this subject's pursuit at MIT, CalTech, Stanford University and further a field. Of course, Endy says "you can't do anything without people", so iGEM is a place where lots of people come together to try to use biology as technology; moreover, he claims that *iGEM is a vehicle for figuring out what synthetic biology is*.

> iGEM is a harvest of opportunity to figure out how you get better at designing a system; how you get better at building it; how you get better at testing it; how you get better at debugging it; how you get better at evaluating whether it's good, bad or ugly; how you get better at sharing all of this stuff; how you get better at talking about it; how you get better at repeating all of that. And that, for me, is hidden often times when people look at iGEM, but it's where it came from as a whole exercise, and it's at the heart and soul of it.
> – Drew Endy, a co-founder of iGEM

Christina notably added, "iGEM's goals have evolved over time". When it started at MIT with Drew Endy, Tom Knight, Gerald Sussman and Randy Rettberg, it was "built around them developing their foundational ideas that they were testing at the time – sort of abstraction hierarchy and common signal carriers and these sorts of

things". What started as getting students to help in figuring out these guys' biological engineering foundations, progressed into something that revolved around designing living systems. Then, upon getting funding from the National Science Foundation (NSF), a multi-school competition began, influenced by the success of robotics competitions. It followed that the integration of more rules about conforming to standards became important in order for the competition to build an open platform for sharing these biological parts, tools and techniques. Now, Christina noted, iGEM's primary goals are about education and community development; to a lesser extent, it remains "partly sort of about building out the foundational technologies". Further supporting my claim, Christina added:

> iGEM is a lot of students' first interaction with synthetic biology and how they get interested in it, and as you saw, not everybody loves it but there's a good number of people that get very inspired and motivated and interested in synthetic biology from this experience. So it builds out a number of people at the younger level that are going to go on and at least try to do something within synthetic biology. It pushes the boundaries there, whether going on to graduate school and research or industry etc. So I think it plays a very important role in at least filling out the numbers at the young level, which are then going to grow up and become part of the older community.

Conclusion

This chapter began by considering judgements that were made during, and shortly after the Jamboree, where projects and broader philosophies were being sold and evaluated. I have shown how everyone is deemed a winner of sorts in iGEM as the competition concluded with an extensive prize-giving ceremony, celebrating several categories and a broad range of accomplishments. Still, deciding on finalists – the very elite teams of the competition who are held up as innovative synthetic biology thinkers and exemplary of the iGEM spirit – involved a great deal of interesting judging politics which, in turn, influence both student and

advisor decisions on joining this community further. Questions around what qualities ought to mark a good iGEM project, making it particularly award worthy, were hotly debated:

- Must projects have a grand vision, a significant and emotionally appealing real-world problem that they propose to solve? Or, are mundane, but useful small accomplishments just as, or more important than (sometimes impossible) 'save the world' ideas? Must teams adhere to BioBricks standards, or will other tools, techniques and stand-alone innovations be celebrated? What qualities of human practices projects might prove them to be more than just a box-ticking exercise?

Additionally, many pioneers of the field feel that this competition serves a particular media-friendly function, believing that its results ought to reflect that – for instance, in having a finalist from each continent to demonstrate synthetic biology's international uptake. Fairness, meritocratic evaluation, practical advances and several other issues were further debated in the iGEM judging circle; the important point remains that *leaders are far from agreeing on what counts as good (and, with what priority ranking) for this competition, or for the field*. When an international community of synthetic biology minds meet (and when there is an opportunity to find out what is contested behind closed doors and in smaller circles) the *early, undefined and evolving qualities of this research area are apparent*.

I have also shown how, at the Jamboree, students are significantly, actively judging themselves, their peers and broader messages. The Cambridge group

deemed that their modest work's winning result spoke volumes about iGEM, disproving some earlier concerns that the competition tended to support more blue sky dreaming at the expense of real science. The Imperial College team was mindful of how their selling tactics set them apart and earned them a prize for human factors; yet, after the competition, I was struck by how a number of these students seemed to reconsider, and take more seriously, an integration of humanities thinking into synthetic biology. Within those two teams and among several other iGEMers I spoke with, I found that (at least, in the short-term), there was an irresistible allure to synthetic biology as the Jamboree delivered countless exciting presentations, parties, motivational speeches and personal interactions with the field's celebrities. Most participants couldn't help but be absorbed by the experience of that weekend and subsequently, they took on board idyllic philosophies about synthetic biology's potential to revolutionize the world in coming decades and often remarked that they wanted to remain part of that community spirit and mission. Additional ideas to attend to from groups such as DIYbio, the FBI, artists and designers, as well as a strong media interest, further heightened the Jamboree's stimulating effects. iGEM organisers have effectively crafted the competition's climax to ensure that students leave feeling deeply inspired in this way – that is why I claim that the Jamboree is a show, not only of genetic engineering, but also *social engineering*.

Though a majority expressed eagerness in wanting to join the synthetic biology club whilst at the Jamboree (and shortly thereafter), I have also shown that, over time, iGEM alumni enthusiasm about venturing into this emerging area waned. As I've followed-up in this community (and particularly with iGEMers from

Cambridge and Imperial College) in 2010 and 2011, informally and through interviews, I've found that most former competition participants look very fondly upon their experience (having learned and developed personally a great deal through it), but chose to proceed within more established fields.

Yet, there remains a significant group of believers who are still chasing a synthetic biology career. Having found that five students from two teams are now pursuing synthetic biology in a more involved sense (through master's programmes, PhDs and work placements) two years following their iGEM experience, it is reasonable to postulate that the competition has enjoyed some effectiveness in its broader recruitment aims. Recall too that the competition has thus far exponentially grown since its beginnings (though it has probably now reached a plateau) and a calculation of 430 teams, having participated in the competition between 2004 and 2010, would entail over 2,500 iGEM alumni students alone[190] – probably a few hundred more participants including advisors and other interested parties. Even if it is only a small fraction of competition alumni who continue in the field, it remains a significant contribution to synthetic biology's development. Additionally, stories such as the 2006 MIT iGEM advisors that have gone on to form Ginkgo Bioworks, which continues to feed iGEM student interns into the company, support an argument for the competition's importance in attempting to help synthetic biology flourish in future. Whether or not the field actually does flourish in years to come is, of course, another unknown matter.

[190] This is assuming teams of about 6 students; generally, the range is from 5 to 12 students, plus 1 to 4 advisors. For iGEM history statistics, see: http://ung.igem.org/Previous_iGEM_Competitions.

iGEM has also been the first seed for several academics around the world to begin growing synthetic biology endeavours in their institutions and countries. With respect to Cambridge and Imperial College, I've explained how the competition sparked these universities' progressive generation of courses, research programmes, funding applications and even the development of CSynBI (the UK's largest synthetic biology facility of this kind). After these leading institutions set this example, many other universities in the UK and across the EU have taken notice and started pursuing the field. Drew Endy and other prominent pioneering figures claim that this phenomenon of synthetic biology spreading from university to neighbouring university, as well as growing in importance within institutions, is traceable globally.

Over the last five or so years, iGEM has helped drive and configure the BioBricks or engineering school-of-thought in this field by producing a wealth of ideas, material realities and followers of this methodology. In this process, a social community has formed – or, more accurately, several factions within this community have formed and co-exist under the same umbrella – and there is a coming together on occasions such as the iGEM Jamboree. This community has a number of compelling founding values[191] that have to do with embracing creativity; fostering a culture for sharing that affords quicker progress; being open-minded and adventurous with ideas across several disciplines; making the world better; and, in being part of this cutting edge biotechnology, prospering financially. However wonderful such philosophies are, they are also not stable and are easily doubted:

[191] Note that sub-groups such as DIYbio have their own more particular missions (described in the previous chapter).

- How far can creative, blue sky ideas really go? Most of the time, the answer is *not far at all*. Projects in synthetic biology that make small, incremental steps forward are the ones that are actually useful.
- Is open source really sustainable when researchers need buy-in to support and protect their ideas in order to take them into development stages? Many believe the open source pot of synthetic biology tools, techniques and materials will have to yield to patent measures as the field develops.[192]
- To what extent are the cross-disciplinary collaborations really working? Many biologists and engineers in this field disagree on their approaches and speak different languages. Many technical practitioners don't want to get involved with social scientists, artists or members of the public – they'd like to simply get on with their work.
- Is synthetic biology delivering on world-saving promises? We await the token anti-malarial treatment out of Jay Keasling's laboratory to be given en mass and, further along the line, we don't know much concrete information about how biofuels research is progressing. There simply aren't many real synthetic biology applications out there, or even in the pipeline, that are discussed in convincing detail or formally publicised.

[192] Desires to increase patenting practices in synthetic biology, even within this BioBricks approach, are evident among some members of this community. For instance, note that the Slovenia 2009 iGEM team patented and did not share two parts.

- It is far from clear whether synthetic biology will continue to receive funding and, in particular, the kind of large-scale corporate and venture capital support that it would take for there to be many people making *serious money* in this field – the kind that goes beyond good academic salaries and might eventually afford private jets (as Randy Rettburg alluded, p. 225).

Across the broad spectrum of those interested in synthetic biology – from its pioneers to iGEMers, from social scientists to artists, from members of the media to government officials – there is a great range in the extent to which people subscribe to the field's ideals and decided to join the club, or not. *Ideas and ideals about synthetic biology are distant from practical realities of both the technical (dis-)order of biology and the social (dis-)order of human beings who naturally have different visions for everything they do.*

As this work's conclusion approaches, I am still compelled to point out recent findings (from the early months of 2011) of a few breaking points that are worthy of further study, but beyond the scope of this work. iGEM's present position is important context: as of 2011, the competition has become too large to be housed at MIT in one final Jamboree, and so has split into regional sub-competitions (Americas, Asia and Europe) that will have separate Jamborees in October; the final Jamboree is to be held at MIT November 5 - 7, 2011, with the top percentage of each region presenting their work to compete for the Grand Prize.[193] Although iGEM has continued to grow, there are several whispers in the community about

[193] http://2011.igem.org/Main_Page; http://2011.igem.org/Regions.

what negative effects this splitting into regionals may have on synthetic biology. Some question whether teams will be motivated to invest the same amount of money, energy and thought to the projects when there is no guarantee of the truly international experience at MIT; some believe that staff will not continue to get as involved and the competition will have to be more student-driven and organised to survive; some are disheartened by the additional organisation pressures and politics in having to adhere to new regional, as well as Head Quarter, rules and preferences. There are several other points of speculation that I won't go into. Overall, I believe one of the most interesting things to track in this change in the competition will be its effects on the already multiple (and often divergent) opinions about what iGEM and synthetic biology ought to value most – something that is suspected to get more complicated with additional levels of regional orchestration[194].

An important division that is increasingly remarked separates *iGEM synthetic biology* from *professional synthetic biology* (and with that, The Registry of Standard Biological Parts versus professional registries such as The BIOFAB[195]). Several iGEM advisors claim that although the competition has been hugely influential for the early years of this field (in educating, recruiting, inspiring, figuring out technical possibilities in this area and establishing a synthetic biology presence in institutions), many laboratories are at a turning point and now want to be considered more "professional" – that is, they have PhD's, post-docs and more

[194] I make this statement with knowledge that there are several different 'traditions' of synthetic biology that are being developed around the world. For instance, in doing research in Japan for a project on international synthetic biology governance, I found that leaders of the field there are much more interested in foundational research (e.g. understanding components of living systems) than they are in building tools and applications (as the ideal focus is in many American laboratories and at CSynBI).

[195] http://www.biofab.org/about.

skilled researchers applying for grants and starting up larger-scale projects to build functional parts, devices and systems. A few thousand parts have accumulated in The Registry since 2003, but there are nonetheless several problems with iGEM BioBricks in that they are poorly described and often not functionally used beyond the initial makers. Most people attribute these significant weaknesses of The Registry to the fact that BioBricks are made by inexperienced students over a short period of time. Despite measures being taken to improve iGEM repository standards, it is widely agreed that professional researchers in the field must separate their work from the amateurs and develop technically sophisticated libraries of parts, devices and systems – whether that is kept in a given institution, or shared among several laboratories. As of early 2011, institutions participating in The BIOFAB collaboration are beginning to indicate that their professional registry is starting to grow; there is, however, still only very limited information on the kinds of biological parts that have been made and used effectively from this source.[196] If indeed synthetic biology is maturing and outgrowing the iGEM level, it is just beginning to do so. As such, there is opportunity to take ethnographic research forward in an investigation of a next phase that synthetic biologists are eager to demark – *from iGEM to professional ranking synthetic biology*.

This maturation, however, is not directed in a uniform fashion given that the community consists in such different disciplines and interests. Several researchers calling their work synthetic biology do not have their hearts set on the BioBricks paradigm:

[196] http://www.biofab.org/projects; http://biofab.jbei.org/services/data/client/.

> Whether BioBricks themselves will develop the field, I think that's more of an open question. I think the standardisation in mechanical parts is a much more straightforward and obvious proposition than standardisation of biological parts. And part of the problem is that biological parts operate in parallel – by that I mean there's a soup and lots of stuff's in the soup and you can't predict what all the interactions are. And specifically it prevents you from really treating things as black boxes because we already know for many of the BioBrick black boxes, they actually re-use the same components inside so you automatically have interaction between them and therefore they're not black boxes and you can't use them as such. So *I don't actually know yet whether the BioBrick paradigm is the right one*. – Frederick, Cambridge iGEM advisor

When technical practitioners are more biology-focused (and realistic about its 'complex soup') than engineering-focused, there are and will continue to be many departures from the project of tediously building and testing possible functional biological parts. A great number of researchers may prefer to take a myriad approach, using what is useful and branching off to find other, non-BioBrick methods that can usefully be employed in their work. I would suggest that an important avenue of investigation going forward would be to note the various adherences to and departures from the engineering approach that has led the early years of this field.

Finally, I'd like to point out finding that there is unrest in the social dynamics in synthetic biology's complex sub-divided community. I've briefly considered tensions that exist between academic versus garage biologists who share attention around safety and security issues, albeit in different ways; other points of disagreement among these camps in terms of what counts as innovation, or the legitimacy of a claim that DIYbiologists must resist the tyranny of established institutions, have also been mentioned. Another relationship worth watching in further research is between artists, designers, synthetic biology professionals and

other interested parties. I am curious whether the intertwining of different design perspectives can help illuminate what might be useful and acceptable in a possible future where humans consume synthetic biology products. A continued examination of media portrayals of synthetic biology[197], as well as government interventions, would be of interest insofar as these players may significantly shape the field's future, potentially posing dramatic challenges and changes in the development trajectory (e.g. in voicing a distaste for synthetic biology, or changing regulations).

There is also opportunity to intervene as social scientists involved with synthetic biologists as these relationships continue to be forged. Social scientists in the US, UK and other parts of Europe have joined the synthetic biology club (in various collaborative networks and initiatives) and have been working with scientists and engineers for a few years now (Calvert and Martin 2009); there have indeed been tensions, not least because the humanities research is almost always a distant second-place to the technical matters at hand, or tokenised in some form, but lessons are being learned and incorporated. For one thing, I believe that a very constructive site for this kind of collaboration is at the level of engaging students who are particularly open minded and primed to think among several perspectives; but this must go further, effectively into the professional ranks, especially if the amateur versus professional divide deepens. It is now crucial that given this opportunity for several interested parties to co-construct synthetic biology's path forward, current and future collaborators must strive to build a more positive, affirmative relationship that will develop this field in a way that is

[197] Media coverage of synthetic biology has started to be examined by researchers at The Woodrow Wilson Center for Scholars (Pawels and Ifrim 2008).

responsive to the realities of technical, social, political, ethical and legal challenges.

The choice now *to join the synthetic biology club or not* is not a simple question. In understanding the kinds of everyday feelings and realities in synthetic biology, there are evidently more people sitting on the fence about diving into this field than is comforting for the evangelists of this subject. There remain several fundamental points of instability in synthetic biology – from what is technically achievable to what will be the dominant socio-cultural messages. This may be too risky for many to bet their careers on; however, for those who do take the risk and join the synthetic biology club, there is still much in formation and as such, plenty of opportunity to help direct this field. That is an exciting prospect for several hundred iGEM alumni and current students of this subject around the world. Beyond filling the wet and dry laboratory positions that will shape this biotechnology, there will also continue to be input from DIY biologists, artists, designers, social scientists, members of governing bodies and journalists that significantly influence the trajectory. If indeed this field does present an opportunity to engineer life for a variety of human ends in the coming decades, how thrilling will be the prospect of involvement.

8. CONCLUSION:
EMERGING WAVES IN SYNTHETIC BIOLOGY AND BEYOND?

This work was originally inspired by an enticing vision of synthetic biology and the opportunity to engage in collaborative conversations that helped to lay technical, social and cultural foundations in this field's early stages of development. After decades of incremental advances in molecular biology, microbiology and genetics, along with the advent of tools such as PCR, DNA sequencing and synthesis and the use of computer modelling in life sciences, we might just possibly be on the brink of witnessing a revolution that could see several elements of the living world engineered anew, aiming to solve pressing world problems with respect to energy, pollution, food and biomedicine. The idea that a true engineering perspective (as opposed to the ad hoc and small scale genetic engineering of previous decades) can be applied to biology, such that a vast array of vital operations can be categorized according to standard parts, devices and systems that obey mechanical rules is captivating to some (although terrifying to others). Of course, this concept of humans mastering and redesigning nature for our own ends is certainly not new (one only has to consider centuries of agricultural practices), but many people are working hard to argue that synthetic biology may present a different paradigm.

However, the story of synthetic biology has yet to be realized by many tangible innovations that convince us of the truth of its promises. I was curious therefore to get behind the popular narrative and into laboratories, observing, participating and talking amongst pioneering practitioners, in order to gauge how synthetic biology

is being taught; how new ideas are dreamed up; what the actual practices and processes are like; and what the social dynamics consist in. Having had previous experience researching synthetic biology (2007-2008), I knew that, especially at the field's relatively immature stage (with very few laboratories having established substantial professional endeavours when I started fieldwork in 2008-2009), one of the most interesting facets was the International Genetically Engineered Machine competition (iGEM). Within iGEM teams, I found not only a site to examine knowledge and material production, but also a place to witness how synthetic biology is a unique feat of both genetic and social engineering. In the early days of this biotechnology's conception and development, a few clever pioneers enrolled their undergraduate students to help them engineer a biological system; seven years later, this has turned into a competition that educates, inspires and indoctrinates hundreds of students so that they help build, and take forward, synthetic biology's technical and socio-cultural foundations. It is a kind of evangelism that converts students to the cause.

Returning to this work's core research questions as they were initially posed:

- How do teams of scientists and engineers imagine, design and build new living systems? What tools for thinking and doing do they employ in this process?
- In this process of knowledge and material production in synthetic biology, how do young researchers transition and rationalise the gaps between the imagined, the designed and the real microbiological machines that they craft?

- How does an undergraduate competition at the heart of synthetic biology seek to ensure the future flourishing of this emerging biotechnology?

This thesis, a work broadly situated in the field of sociology of scientific knowledge, thus concerned the process of idea generation and its evolution into design and experiment that eventually generated new knowledge and material forms. The incubation of this trajectory was situated in layers of socio-cultural dynamics. In Chapter 2, I presented the case why, methodologically speaking, it was necessary for me to be observing and participating directly in the field in order to unravel the processes of interest. From Chapters 3 through 7, this work has gradually built that story of knowledge and material production, observing two core teams and adding the layers of social complexity that accrued as there was the addition of advisors and affiliates, an institutional culture and a global community of players with a variety of goals and visions for synthetic biology.

Summarizing this thesis' major arguments, I begin with 'Dreaming up ideas', in which the story of how Cambridge and Imperial College iGEM students were taught, and how they came to conjure up project ideas, presented a convincing case that the early stages of a synthetic biology endeavour are highly *creative*. I made use of the Bachelardian (1984) notion of phenomenotechnique to describe an act of the scientific spirit that is not particularly hypothesis-, discovery- or deduction-driven (as the pursuit of scientific knowledge can often be described); rather, dreaming up ideas in synthetic biology is first an imaginative exercise in the mind, before rational processing of design and execution possibilities can go on. This creative exercise also had a technology- and application-driven bend,

right from the beginning. Furthermore, dreaming up ideas is not abstract insofar as students extensively used tools for thinking such as drawing mind maps, making lists, sketching pictures, using online forums and conducting presentations. Such media gave a materiality and ontological status to thought – they served as a point of attachment upon which ideas could be understood, extended and re-worked by teammates and advisors.[198]

Dreaming up ideas is not only about phenomeno-techniques in operation, making use of intellectual technologies (Miller and Rose 1990) that materialize ideas so they can evolve; the way in which students thought of possible projects was also highly influenced by how they were taught to understand synthetic biology and iGEM. At Cambridge, the crash course was crafted to introduce all students to the basics of this biotechnology, but it did so in a particularly inspiring way – lectures were animated and filled with appealing analogies (Lego™, electronics industry development, etc.); workshops from designers as well as guest appearances from entrepreneurs and a computer scientist at Microsoft kept things interesting; and laboratory practicals were playful, showcasing the best of synthetic biology ideas (e.g. the banana and wintergreen smelling bacteria experiment, working with Arduino kits, etc.). This group's initial two weeks of sparking creative interest meant that they were somewhat primed to the difficult task of facing a blank page, considering a massive biological library and thinking about how to apply

[198] Other laboratory ethnographies, notably that of Latour and Woolgar (1986 [1979]), have also brought to light an obsession that scientists' have with various writing practices (on black-boards, drawing pictures, creating graphs and charts, etc.). Latour and Woolgar's (ibid) concept of *literary inscriptions* shares some interesting similarities with what I've described about the mind maps, experimental protocols, etc. of iGEMers; however, as noted in the literature review, Latour's (1986; 1987) specialized inscription, the *immutable mobile* doesn't fit well with the *especially mutable* nature of synthetic biology's inscriptions and descriptions of existing entities and practices, new hypotheses or new entities.

synthetic biology rules in order to craft a microbiological machine. The Imperial College team members did not all partake in an introductory course to synthetic biology; rather, a series of try out meetings shaped and unified a particular pattern for the group's thinking. Students learned early that, in their institution's tradition, iGEM project pitches ought to demonstrate grand-scale, problem-solution oriented thinking; they ought to show a clear adherence to a modular, engineering approach; yet, they still had to offer competitive deliverables. The bar was set very high from the beginning and the team focused their formation of ideas around the advice of their supervisors.

In the iGEM experience, the initial educational and inspirational framing that takes place is probably quite specific to a given team and their advisors' and institution's driving values. Still, there are significant features that unite over a hundred teams' iGEM experiences in a given year – most importantly, each team receives the same standard BioBricks from the Registry and generally follows the parts-devices-systems school of thought. These standardization practices play an essential role in unifying synthetic biology (to some extent), giving the field's practitioners a sense of collective creation of standard theories, tools, techniques and components for going about their work.[199] Although there are such large-scale group efforts helping to coalesce what synthetic biology is about, I was somewhat more fascinated by the differences apparent in localised groups of iGEM teams and their advisors. At the introductory, microsocial scale, there are only a small collection of people at the heart of dreaming up an idea for a synthetic biology project. The specific knowledge, virtues and goals of individuals significantly

[199] Recall from the literature review echoes from Fujimura's (1996) study that demonstrates how standardization of theory and methods played an essential role in the co-construction and growth of proto-oncogene research.

shape the possibilities of a team's dreaming. I suspect that this feature is shared across several domains of innovative thinking. Whether a team is aspiring to design a new iPhone App, a medical device or a biosensor, the motivations of the characters involved, their curiosities, beliefs, talents and broadness of outlook, are all crucial in determining the boundaries of thought.

In Chapter 4, I described the teams' transitioning from *thinking about synthetic biology* (a world of ideas) to *doing synthetic biology* (a world of practical design, experiment and computer modelling). The evidence points to this transition not being a smooth one partly because there are conflicting understandings of synthetic biology as a field of effective, discrete engineering (in theory) but also one that frequently faces impenetrable complexity in living systems (in practice). Nonetheless, teams forged ahead, and after arriving at an idea that stuck – to build a colour-producing microbiological machine (Cambridge) and a self-encapsulating drug manufacturing system (Imperial College) – they dived into a set of wet and dry laboratory practices. In doing so, both teams found that many protocols were not streamlined as descriptions of synthetic biology often present. There was a great deal of tedious work, which involved small volumes of clear liquid and lots of waiting time. Many cycles of failed experiments had to be repeated and there was lots of returning to the mind map-style drawing board.[200] The major work of the dry lab was to model various aspects of the biological systems under construction (rates of reaction, changes in the system over time, etc.), which gave the teams some nice data for presentation; additionally,

[200] Recalling the literature review's descriptions of other laboratory ethnographies, I found the Cambridge and Imperial College laboratories in their experimental stages to be similarly full of failure, highly contingent and somewhat mundane. Knorr-Cetina's (1981; 1983) concept of *making thing work* as well as Fujimura's (1996) concept of scientists constructing *"doable" problems* both resonate with my findings in observing the iGEM teams processes.

modelling was sometimes used to input hypothetical data when experiments didn't go as planned so that students could at least build a proof of concept case for missing components of their project. Perhaps the most exciting venture in the mid-phase for both teams was to design and order gene constructs online, which were synthesized by an outside company and sent back to their laboratories in the post. The Cambridge team's violacein construct that year remains one of the most ambitious synthesis endeavours that the iGEM competition has seen. So it is true that, mixed with old methods and failed experiments, there was some very exciting synthetic biology technology used. The ability to cut and paste a desired gene sequence into a computer programme, make some artful (and well-researched) changes to that sequence so it would function better for a given purpose; being able to then click send and receive synthetic DNA in a FedEx package a couple of weeks later, ready to be incorporated into an experimental living system – an impressive feat.

What is important to highlight in conclusion about this design and experiment phase is that it was where I found the most candid discourse about, and display of, synthetic biology's *present reality*. Practitioners in this field may all believe that there are numerous exciting ideas to be imagined and tried; they might also hold that an engineering framework is the key to taking this strand of biotechnology to an industrial scale (though there are many variations on this view). However, the reality of everyday design-experiment-fail-redesign (and so on…) cycles serves as a sobering reminder that the foundations of synthetic biology were not then (when I was in the field in 2009), and are not yet (2011), stable. Many experiments don't work out as planned because many BioBricks from the Registry don't function

reliably. Presently, engineering that is accomplished with BioBricks in one lab and described in a standard fashion, certainly does not guarantee that the same result is reproducible in another lab. In the iGEM context, projects required a great deal of scaling down from their initial visions in order for any tangible results to be achieved. Because students were often disheartened by experiments not working, I frequently witnessed advisors comforting them and telling a more grounded story of what is achievable in iGEM and, more broadly in synthetic biology, given the field's immature state. Recall this poignant consolation to the iGEMers, from Cambridge advisor Frederick: "It's OK, it's not necessarily you; it may just be that the molecules don't want to do that and that's the way it goes".

Molecules not wanting to line up a certain way; a strand of DNA that is rendered non-functional due to one very small change in code; bacteria that die with the introduction of a gene that produces a compound not native to that species; a vial that is shaken too much, or not shaken enough; an experimental specimen left at a slightly less than ideal temperature for one minute too long – such seemingly small things separate operative elements of life from inert or useless material. Vitality persists only in a delicate balance. Yet, synthetic biology pushes the very boundaries of vitality, wondering what new designs and combinations of nature's mechanics might yield (fuel, medicine, sensors and remediators, art…). It is at this boundary, and when ideas turn into experimental practice, that Canguilhem's (2009) reference to the '*vitality of vitalism*', the '*fecundity of vitalism*' and the '*character of honesty in vitalism*' has an important place. Canguilhem's work articulates changes in biological theory throughout history and takes special notice of repeated returns to vitalism. For him, the rebirths of vitalism translate "life's

permanent distrust of the mechanization of life", where one finds "life seeking to put mechanism back into its place within life" (ibid, 73). Canguilhem's (2009) vitalism is a philosophy rather than a mode of scientific thinking, something of an ethical cue rather than a working theory. Bringing vitalism into a discussion around synthetic biology is not about the persistence of a mysterious vital force; given that today there is undeniably a great deal of knowledge and control at biology's molecular scale, support for a reductionist and mechanistic view of the living world seems to defeat rather archaic-sounding theories of vitalism. Nonetheless, as a philosophy, vitalism has its place today, reminding us to not only recognize the limits of our understanding and engineering ambitions with respect to the living world, but also to undertake a broader reflection on how biotechnology practices shape a society's philosophy of life.

Rose (2011) recently argued that, in light of Canguilhem's work, we must remember that, "every mode of biological reason is also, in a certain way, a philosophy of life". For Rose, "our way of living, our sense of how we should live as humans, why we should live as humans, of what we owe to ourselves and others, of what we can know, of what we can do, what we can hope for – all of these have become tangled up in what we think we are as living creatures and what we think about our relation to other living creatures in the world in which we inhabit" (ibid). With respect to synthetic biology, vitalism not only brings in the obvious concepts of life's complex, dynamic, evolving, reproducing, sensitive qualities that entail a resistance to being re-engineered, but it also prompts a reflection on what might be humble limits as practitioners continue to develop technologies that remake life (slow as that process may be). These limits ought to

be responsible to social morality – a broader philosophy of life – and considering them can be a key impact of the cross-disciplinary engagement that is occurring between synthetic biologists, social scientists, artists and designers.

Returning to the narrative, recall that another activity that did not transition smoothly from the idea stage to the doing stage was in getting the Imperial College human practices project off the ground. Although there was initial support from a couple of advisors when I first proposed to help the team with this idea, as time went on, the side-lining of such an exercise was evident when compared to the need to get real experimental results churned out as the team felt behind, with pressure mounting. Yet, with the help of an inspired student (Andrew), I was able to accomplish, in one day, the orchestration of a workshop and interviews with every team member; together, Andrew and I proceeded to make the human practices video and write a summary document about this side project.

Collaborations between synthetic biology practitioners and humanities scholars – though desirable, celebrated and funded – remain in uneasy territory. Some synthetic biologists are weary of being the subjects of a study; others show their belief in science and technology's moral authority over different forms of knowledge; and still others are just not interested or don't see the advantage in really engaging with ideas from the humanities or artistic fields. Such feelings certainly present challenges for the involved social scientists, yet, for the time being, there remains a window for this type of collaboration. Having witnessed a number of meetings and been involved directly in this community over three years, I have hope that practices and values inherent in synthetic biology have

been, and can continue to be, mutually shaped by perspectives from life sciences, engineering, humanities, government, publics, art and design. I believe the kind of multifaceted and integrated making of this biotechnology is most fruitful among those still in education – those participating in iGEM (including in an advisory capacity) or in university courses – as there are often open, inspired and excited frames of mind in such spheres. Interestingly, there is also a good deal of collaborative outreach from the DIYbio community, particularly with public audiences (though I have not been able to examine it in detail). On an inevitably bumpy road, synthetic biology stakeholders in every discipline are learning from experiences as they go along, hopefully building some relationships that will take this field forward in a manner that is especially mindful of a broad range of societal, regulatory and ethical concerns.

Another important gap between synthetic biology theory and synthetic biology practice that was illuminated is that there is no seamless merging of biology and engineering perspectives (as is sometimes presented). In reality, different disciplinary perspectives (loosely categorised in camps of biologists and engineers) struggled with technical language barrier issues. More broadly, we can analyse these boundaries as distinctions in styles of thought. Biologists tended to have, or sought out, explanations of biological complexities; though this activity could lend insight into why some experiments did not work, it tended to confuse and frustrate engineers who wanted some good data crunching material so they could build the models, graphs and predictions that they enjoy. Only a couple of exceptional students at Imperial College sought to *really* learn more about (and practice) the other disciplines that were not in their previous training. Most

biologists did more of the wet lab work and most engineers stuck with their computers and differential equations. Rather than a merging of disciplines, synthetic biology practice here was more about each individual finding a way to contribute their knowledge and skill-set to the tasks at hand. The different views about synthetic biology ideas, ideals and practices that were divided between biology-leaning minds and engineering-leaning minds was a highly significant observation that came up again in the selling and judging stages at the Jamboree.

In Chapter 5, the narrative shifted and examined what kinds of entities were actually made real in E. Chromi and the E.Ncapsulator. I found that, given the limited time frame and various set-backs, although the teams developed an idea for something that would qualify as a whole biological machine – an arsenic biosensor that would have programmable sensitivity tuners as well as easy-to-read colour outputs (in the E. Chromi story) and a drug manufacturing and delivery platform that would allow a chemical synthesis of choice, targeted delivery of that compound to the gut, plus a guarantee that the bacteria had 'committed suicide' before consumption (in the E.Ncapsulator story) – they could actually only build parts of these overall systems and make some additional proof of concept cases with hypothetical models. It is important to emphasize that the chance of constructing a fully functioning, synthetic biology-driven machine remains slim in the scope of iGEM. Still, both teams' accomplishments were remarkable, including colour generators that vividly produced brown, purple, green, orange and yellow outputs as well as an engineered *E. coli* that evidently coated itself in a protective colonic acid layer, increasing the cell's resistance to acid degradation and therefore protecting its contents.

Understanding the kinds of material entities that were actually produced, I made use of two areas of discussion in order to question how we might think of, name and categorize synthetic biological machines. Firstly, I invoked Hacking's (1983) position as a 'realist about entities and an anti-realist about theories' that considers experimental entities *real* when they have been created, produced, refined and used with respect to other experimental materials with known cause and effects. I claimed that although there is good reason to doubt the truth of synthetic biology's theory or project ideas, once the move to experiment takes place and some new material forms clearly display intentionally engineered causal properties – such as the purple producing bacteria, or an *E. coli* that coats itself in acid upon a particular trigger switch – then we have good reason to believe in the realness of such entities. With this argument, I highlighted that despite having unpacked a number of social dynamics (e.g. about character roles, tensions between disciplines and institutional cultures) throughout the narrative, has not been my intention to build a case for the social construction of scientific knowledge and artefacts.

I aimed to present an accurate picture of the practices and processes that generate ideas and entities in synthetic biology; and, once we do see materials being made, and we witness their causal potentialities, I think taking a position and labelling such things as social constructions is not terribly illuminating. Like Latour and Woolgar's (1986) move in removing the word "social" from the subtitle in the second edition of *Laboratory Life: The Construction of Scientific Facts*, I too rather avoid confusion, and leave aside the words "social construction" in

describing the resulting entities of genetic engineering. All truth claims and human engineered entities have social factors that shape their possible existence; as such, they can be described in terms of a social constructionist line of argument. There are of course several social constructions operating in synthetic biology laboratories. However, in my argument, I have intended to step outside the social constructionist debate, and attend to lessons specifically inherent in synthetic biology. Biologically engineered entities that have causal properties, that are capable of being affected by and interacting with other entities in a milieu, ought to be treated according to their real material potentialities. In the case of a biosensor made with synthetic biology parts, this consideration entails attending to important matters such as the safety and functionality of a machine. Just because the construction of the entities in synthetic biology involves a social process and many contingent ways of interpretation and ascribing meaning, it is not reason to cry 'social construction' and stop there. The point that real things are constructed in complex, risky and specific ways – and that such things could continue to be complex, risky and involve other yet unknown specifics when they are pieced together with additional biological parts or situated in different environments – needs to be taken seriously. Social scientists must be careful to attend to the biology itself, just as we ask that synthetic biologists attend to our presence and our research concerns in a serious and rigorous fashion.[201]

Thinking about the materiality of synthetic biology systems, I also raised some of Canguilhem's (2009) ideas about machine and organism. Might these ideas help individuals formulate a view on the categorisation of present and possible future

[201] This attending to the materiality of synthetic biological entities that I am calling for is, in some ways, along the same lines of argument developed by the new materialists (for instance, Bennett and Connolly 2002; Bennett 2004; Barad 2008).

synthetic biology's outputs? If, according to Canguilhem, machines obey calculations, are rationally designed and function predictably, and organisms have endless latitude, behaving as "an attempt in all directions" (ibid, 90), then what are we to make of a new, intentionally engineered, mechanical organism? In the end, I raised these questions but do not believe we need to precisely define a novel breed of synthetic, mechanical organisms at this time. Synthetic biology remains a young field, and though its ambitions for creating synthetic life can sound like lofty, scary Frankenstein science, I think its current outputs of discrete biological parts and systems is, for the most part, not terribly dramatic or worrying. Nonetheless, the subject of engineering life in the 21st Century has profound social and ethical implications that we should attend to and debate. Moreover, I have argued that a continuing conversation among many interested parties ought to seriously consider present realities of everyday laboratory practice. Real stories, with real people, showing the sorts of things that this field is actually doing are critical – not only to avoid indulging overly fantastical narratives (good and bad) but also to provide valuable insights about entry points for those who want to get involved in shaping synthetic biology's future.

This study moved from the UK to the international Jamboree stage in Chapter 6 and presented two sections of empirical data that helped answer how this competition has sought to support a flourishing future for synthetic biology. The Jamboree context was the first important layer: with its dramatic location (the spaceship of the Frank Ghery building at MIT), spirited Halloween timing, the high profile attendee list of synthetic biology V.I.Ps, interested groups on the fringes, American-themed parties and colourful displays of team pride, it is no

wonder that the event is coined *the Olympics of amateur genetic engineering*. The backdrop of the finale created an ideal atmosphere that served to excite, inspire and sell synthetic biology projects and philosophies to hundreds of undergraduates, many of whom aspire to be future leaders in this field.

The second section of Chapter 6 detailed the sorts of projects and ideologies that were vibrantly on display at the Jamboree. Teams had their twenty-minutes to shine in front of a peer audience and several judges: they explained their aspirations to solve a given problem, showed off their most impressive results, likely exaggerated a few points, admitted to some setbacks and orchestrated their best version of a competitive and engaging presentation. Highlights such as ArtScience Bangalore's intriguing 'smell of rain' project, or the 11-year-old's BioBrick-A-Bot and a high school team's building of their own lab kit reflected the open-minded and adventurous spirit of iGEM. Teams were also busy selling their projects through poster presentations, cartoons on blackboards, mascots, give-aways, team T-shirts and the like. The active pitching that competitive teams were doing was matched by more established leaders' roles in selling back to students a number of synthetic biology's idyllic philosophies (worth repeating):

- This community is revolutionary in its open source ethos that supports collaboration as well as work from amateurs and lesser-funded laboratories;
- This community believes biotechnology will make the world a better, cleaner, healthier place in the coming decades – we are now in The Century of Biology as Technology;

- This community consists of friendly and outgoing contributors whose expertise cross several disciplines – from all walks of science and engineering, to humanities, art and design. This community is not represented by stereotypical images of reclusive scientists; rather, it is represented by a mix of clever, vibrant and playful characters;
- Finally, dedicated researchers who enter this up-and-coming field will prosper financially for their incredible work to come. Most notably, this point came through in the closing speech of iGEM Director Randy Rettburg when he announced, "I think that over the next 40 years synthetic biology will grow in a similar way [as the computer revolution] and become at least as important as the Internet is now and that you will be the leaders, that you will form companies, that you will own the private jets and that you will invite me for rides".

The fact that the Jamboree was also host to non-competitive, but nonetheless interested parties, who had their own messages or stories to seek out – I'm referring to groups such as DIYbio, biotech representatives, government officials, designers, journalists, film-makers and social scientists – served to increase this sense of synthetic biology's general significance as a key, budding 21st Century technology. All of this information serves my argument that the competition is designed to help inspire (and in some senses, socially engineer) its participants to want to jump on the synthetic biology bandwagon, in order to develop this field in years to come.[202]

[202] Note that Fujimura (1996) similarly discusses the creation of an oncogene research *bandwagon*, which, in her study, is a configuration held together primarily by the standardization of experimental systems, tools and packages that enabled practices and theories to be shared and passed between participants across several social and disciplinary spheres. Similarly, the synthetic biology bandwagon is, in part, held together by shared practices, standards and an over-aching theory for the field (parts, devices, systems, etc.); however, what I've shown to be equally

It is important too to mention another gap that becomes apparent as teams move from working at their own institution's laboratories to the competition stage. Although the vast majority of projects would not have turned out as teams hopefully envisioned, they eventually land at the finale and find themselves presenting in front of hundreds of peers and an impressive list of judges. In this transition, the grounded conversations that may have easily been had in home laboratories weeks earlier (about synthetic biology's pitfalls) were abandoned; students and leaders find the Jamboree an occasion to sell, spin and hype ideas and ideals. This again serves the purpose of generating an alluring ambiance over that weekend, but it does not reflect an accurate picture of what synthetic biology entails in the day-to-day.

Chapter 7 continues to support my argument that iGEM is a tool to educate, inspire and indoctrinate a next generation of researchers who can help take this field forward; however, the follow-up data presents a mixed picture and it is important that the nuances come through. All participants of the Jamboree evaluated team projects and broader ideals in some way and these judgments shaped decisions to join the synthetic biology club or not. During and shortly after the Jamboree, most students inhaled an air of inspired buzz – they sounded keen to join. After some time and distance, reflections about pursuing synthetic biology seemed to become more tempered for most students and many decided against going into further studies of the field. This point is worthy of a little elaboration in conclusion.

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important, or perhaps more important, in the synthetic biology bandwagon, is a kind of social and political rallying that in the processes of 'selling ideas' and choosing to 'join the club, or not'.

Forging a new interdisciplinary field is easier said than done. In practice, the extent to which people want to themselves become true cross-disciplinary experts, as well as their comfort levels in leaping into the unknown[203], have their limits. There is a riskiness involved, with uncertainty about whether a new discipline may blossom or fade out – understandably, individuals may feel hesitant identifying themselves with a field that will inevitably make many mistakes in trying to define its scope. When a synthetic biology team is mainly composed of members trained in established fields of engineering and life sciences, there is a sense in which people like the idea of being part of this emerging, exciting field (especially at events like the Jamboree); however, they also tend to want to keep one foot firmly rooted in their original discipline. It is exceedingly difficult to satisfy, or settle, a broad range of views on what synthetic biology is. The frustration involved, I suspect, has some people turning back to their original discipline, where there are perhaps more stable jobs, research and funding trajectories – or, at least where the territory is more familiar. It takes courage and a leap of faith to dive whole-heartedly into a new area. The case studies I have presented show that some participants who have appeared to dive in, have actually later chosen to step back into engineering or biology comfort zones a couple of years following their iGEM experience.

[203] I refer to a sense (explained by many participants) in which, in the case of synthetic biology, its so-called 'merging of biology and engineering' (two independently established fields) leaves it in unsettled territory. Is it more biology, or more engineering? Does bringing the disciplines together entail something entirely new? Or, is it merely an awkward mixing of established practices and philosophies? What exactly this field is about can be difficult to articulate, especially when it is held in comparison to one of its more strongly defined composite disciplines.

Still, there are a few specific stories and a notable trend of uptake of iGEM alumni deciding to join the synthetic biology club that remains impressive. I have described how previous MIT iGEM advisors went on to found Ginkgo Bioworks and illustrated how the progressive growth of the competition over the past seven years has led to several universities starting synthetic biology endeavours (in, for example, developing courses and even full-fledged research centres). iGEM has undoubtedly been a very significant influence in spreading the word of this emerging biotechnology to all corners of the globe. In the groups that I've followed, there are at least five students currently striving to be part of a next generation of synthetic biologists. Overall, the competition has now educated and inspired well over two thousand students, advisors and faculty, a portion of whom will still be actively participating in the broader field, hoping that its future delivers something substantial of its present (mostly not realised) promises. Undoubtedly, iGEM has been a remarkable site for amateur genetic engineering that has worked out many early-stage ideas about what synthetic biology ought to be about; moreover, it has been a unique phenomenon in the landscape of today's emerging biotechnologies[204] with respect to its ability to socially and culturally influence a number of people, committing them, in some sense, to be promoters of this new field.

This summary of arguments has detailed major points from Chapters 3 through 7 that specifically work to answer the core research questions outlined above. I have

[204] There is no analogous competition to point to other recent developments in the neurosciences, nanotechnology, stem cell research, etc. Although the iGEM competition was, in part, modelled on the success of various robotics competitions (look, for instance, at http://robots.net/rcfaq.html) – something I do not know much about and will not comment on – its effect in recruiting involvement to synthetic biology's cause is, to my knowledge, intriguingly unique. What combination of characters, timing, powerful rhetoric, larger social phenomena in open source collaborations, etc. made this happen is an interesting matter of conversation.

also explored other interesting, sometimes slightly tangential, findings from the field. Throughout the empirical chapters, I developed a flavour of many characters behind the story that was developed. Early on, I wrote about the striking leadership found in Emma (Cambridge), the development of Senni's great scientific skill (Cambridge), Andrew's curiosity in philosophical discussions (Imperial College) and Nisha's tremendous teaching talents (Imperial College). I developed a sense of who the advisors to these teams are, and what they valued about iGEM and synthetic biology: the hugely devoted Andy; the patient fountains of knowledge found in Samuel, Geoffrey and Frederick; the tough love spirit of Roger's advising; Bernard's bizarre ideas about the importance of emotional appeals that ought to be attached to competitive projects; Max's and Olivia's devotion to helping students in their most trying of moments in the wet lab. These characters and their relations to one another all evolved over the course of the summer, as did my relations with participants (detailed in Chapter 2). I also explored institutional cultures, various values and mission statements of numerous sub-groups – from the traditions at Cambridge and Imperial College to the perspectives of DIYbiologists, biosecurity officials and designers attempting to provoke reflections about this field's future implications. iGEM 2009 proved to be a hugely important experience of personal development for the great majority of individuals I interacted with, and for myself as a researcher.

Before moving to a few broader conceptual thoughts, I'd like to emphasize that a large part of what this thesis has done is to capture a detailed narrative of knowledge and material production as well as the surrounding sociality, that took place in a relatively short window of time, among pioneering synthetic biology

practitioners. I have only been able to illustrate a small part of the life cycle of iGEM, and synthetic biology's development. This field is actively changing – in its technicality, tangible outputs, social structures and ideologies, size, relations to governments and publics – and with that, some of this narrative is set in historical bounds. In that sentiment, I present a final figure below, picturing the two teams and I at the conclusion of the 2009 iGEM Jamboree.

Figure 8.1: An ethnographer embedded in winning teams

Photos attributed to iGEM and David Appleyard.

Yet, there remains a broader set of conclusions and open questions that this work speaks to. I would like to now, in closing, share a few reflections on the nature of innovative knowledge production and an understanding of life.

The notion that developing a new area of technology must first come from a set of imagined possibilities in an exercise of 'dreaming up ideas' has been an important theme in this thesis. It is an interesting finding that even in today's highly scientific and engineering-driven fields – associated somehow with sterility, high-level molecular control, concrete facts, robotic practices, computerised precision, black-box descriptors and the like – people are creatively imagining, mind mapping, sketching out loose ideas and reaching into virtual communities; they are grappling with a mix of languages in often conflicting frames of thinking and doing; they stumble along and try to find a way to bridge several gaps. Innovative knowledge production can, it seems, arise from a rather messy landscape of thoughts and social interaction. I now wonder: might an iGEM-style of imagining ideas be indicative of some broader characteristics of contemporary innovative science?

David Edwards, founder of Le Laboratoire in Paris[205], believes that there is gathering momentum behind a process of ideation and product generation that is driven in a creative, highly interdisciplinary fashion – something, he says, happens best when conventions and boundaries between science, art, design and culture are broken down (Edwards 2010). (Apparently, Edwards' teams of scientists, artists, designers and entrepreneurs can be found dreaming up their ideas in a circular room, encapsulated with white boards, equipped with several colours of marker for complex drawing, as well as bean bags and a log for quiet moments of contemplation.) In reading Edwards' (ibid) book, it strikes me that

[205] Le Laboratoire is an experimental science, technology, art and design laboratory, shop and exhibition space in central Paris "where creators and society meet through cultural exhibition, a new platform for innovation" (Edwards 2010, 3-4). Also note http://www.lelaboratoire.org/en/.

there is a notable collection of sites for idea incubation where doors are being opened to incorporate a wide variety of views – sites such as iGEM, Le Laboratoire, École des Arts Politiques[206], SymbioticA[207] and even much larger companies such as IDEO[208]. Though I cannot claim to understand the workings of all such organisations, perhaps they show parallel opportunities in which many interdisciplinary perspectives are included, not only to ideate and create real things but also to assess critically what should and should not make a transition from idea to reality. In some spheres of innovation – right at that early stage of furious idea generation, extraction of the pursuable project and transitioning to a process of design, experiment and making real – one can find life scientists, engineers, artists, designers, entrepreneurs and social scientists.

Whether or not ideas in synthetic biology (and under the broader umbrella of bioengineering) get made real is, of course, also a matter of the extent to which biology is amenable to our designer wishes and technical ability. The stuff of life mostly shows its recalcitrance at the point of physical intervention. Biology, more than any other material one can attempt to shape and re-make, defies being tamed, black-boxed, engineered. What an empirical story of knowledge and material production in synthetic biology currently highlights are limits to what we can create. Those many views involved in shaping what ideas are dreamed up and

[206] Founded by Bruno Latour in 2009, École des Arts Politiques, is an innovative educational institution that connects the arts with a broad range of social and natural sciences (http://speap.sciences-po.fr/en.php?item.8).
[207] Founded in 2000 by a cell biologist, a neuroscientist and an artist at the University of Western Australia, "SymbioticA is an artistic laboratory dedicated to the research, learning, critique and hands-on engagement with the life sciences" (http://www.symbiotica.uwa.edu.au/).
[208] IDEO is a design consultancy firm, renowned for its human-centred approach that develops a wide range of products, services, processes and strategy (http://www.ideo.com/about/).

attempted, I've suggested, can voice this limit; however, ultimately, biology decides.

Living entities are situated in layer-upon-layer of milieu: DNA (in BioBrick form or otherwise) operates only with a host of cellular machinery, in a complex chemical soup; multiple cells clumping together (whether from the same organism or many independent unicellular organisms) take on a whole new set of functional properties; and so on, to the complexity of human beings and our interactions with each other and the rest of the living world. With every additional environmental layer, living entities exist under a set of conditions that become harder to comprehend. Biology is inherently difficult to define and characterize; it is unpredictable, unwieldy, reproducing and struggling to persist through evolution. Even if one believes that living entities are mere composites of purely physical and chemical properties, their vital organisations and mechanics, in many respects, remain mysterious, perhaps unknowable.

Whether or not we will ever categorically add a branch of *Synthetica* on the Tree of Life, and what those organisms might consist in, remains to be seen. In the coming years and decades, as approaches and possibilities in engineering biology change, what we can do, as Rose (2007) suggests, is continue to map a "modest cartography of the present" that shows our living in "in the middle of multiple histories" with a conditional present and an open future (5). Moreover, one can seize the opportunity to intervene and act in collaboration to help dream and make up our living world.

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APPENDICES:

Appendix I
Research Information Sheet
Human Subjects Consent Form
Further Agreement

Appendix II
Intellectual Property / Open Source: supplementary excerpts

Appendix III
Imperial College 2009 iGEM team Human Practices project: supplementary documents

APPENDIX I

(i) PhD Research Information Sheet

This sheet was given to research participants to keep. It was purposely designed to be user-friendly and cater to the mostly undergraduate student population that was involved in this ethnography.

GOING SYNTHETIC: HOW SCIENTISTS AND ENGINEERS DREAM A NEW BIOLOGY INTO REALITY

Who am I? The researcher:

- Caitlin Cockerton: Current sociology PhD student exploring synthetic biology, supervised by Prof Nikolas Rose and Dr. Filippa Lentzos, BIOS Centre, LSE
- 2008: MSc Biomedicine, Bioscience and Society, LSE, distinction and top of class
- 2003-2007: BASc, McGill University (with study abroad at University of Edinburgh), double major in microbiology and immunology as well as philosophy

What am I researching? Why is this research important?

- In 2009-2010, I will conduct fieldwork to examine how iGEM teams design and build a biological 'machine'. I want to explore how iGEM inspires interest in synthetic biology and gives space for students to dream, model and fabricate new biological entities.
    - What is at stake as synthetic biology tries to take its place as the latest productive stream of biotechnology? Is the application of engineering to biology really analogous to engineering as applied to nuts and bolts, electronics and computers or the construction of bridges?
    - Might synthetic biology evoke a change in how human beings and social practices understand biology (and what it is to be a 'living organism')? How might human interactions with the 'biological world' be altered (if at all) when dealing with biological forms that are 'synthetic' and constructed from scratch?
    - What might a social scientist learn from paying close attention to the way in which synthetic biology requires its innovators to imagine, design and then construct new biological (even 'living') units? *Investigating how the dreams of scientists and engineers evolve into reality is profoundly interesting at a sociological level.*
    - *I am also interested in the extent to which the new ways of thinking about biology in synthetic biology might percolate into social life and culture more generally.* For example, Darwin's theory of natural selection and the 'gene for' idea both had consequences far beyond biological research.

What will this involve?

- I will focus on two elite UK teams and trace the groups' project development from the beginning stages to the aftermath, following the iGEM Jamboree at MIT.
- I will primarily use ethnographic methodology, observing and participating amongst iGEM participants (03/09-12/09). Notes and selective recordings will serve as data.
- Ethnography will be supplemented with semi-structured interviews, both in groups and in one-to-one formats. Interviews will generally be recorded.

How will the data be used?

- Research data will be used in writing my PhD thesis; however, it may also may be blogged online, discussed at conferences, published in a book and in academic journals.

Will your input be anonymous?

- Interviewees will complete a consent form; a choice is available to remain anonymous or to have one's name and/or occupation written in my work.
- Interviewees have the right to stop participation in an interview at any time or ask the researcher to have segments taken 'off-record'.
- I will be holder and interpreter of the research data; however, upon request, data can be accessed by participants.

Further questions? Please do not hesitate to contact me:

Caitlin Cockerton: c.cockerton@lse.ac.uk

(ii) Consent form

This was the consent form I gave to participants and received signatures for.

HUMAN SUBJECTS CONSENT FORM 2009-2010
Going synthetic: how scientists and engineers dream a new biology into reality

Caitlin Cockerton,
PhD Candidate, BIOS Centre
London School of Economics and Political Science
http://www.lse.ac.uk/collections/BIOS/
c.cockerton@lse.ac.uk

You have been asked to participate in research conducted by Caitlin Cockerton, PhD candidate at the BIOS Centre, The London School of Economics and Political Science. The purpose of the research is to explore the process in which iGEM teams formulate their summer project and work towards building a synthetic biology 'machine'. The research will be taking place in 2009-2010.

PARTICIPATION AND CONFIDENTIALITY

Your participation in the research will involve informal participant/observation interaction with Caitlin Cockerton and potentially being involved in interviews (group or one-to-one). Caitlin will be taking notes and making selected recordings. You may choose to remain anonymous, but Caitlin will ask permission to use your name and/or occupation in her work (below).
Results of this research will be used for Caitlin's PhD thesis at The London School of Economics and Political Science. In addition, results may be blogged online, published in a book, in academic journals and discussed at conferences.
Caitlin Cockerton will be the holder and interpreter of the research data; however, upon special request, data can be accessed by participants. You have the right to stop your participation in an interview at any time or ask the researcher not to record.

PLEASE TICK ONE

[ ] My name, occupation and institutional affiliation can be written in Caitlin Cockerton's work.
[ ] My occupation and institutional affiliation can be written in Caitlin Cockerton's work; however, I would not like my name used.
[ ] I would like to remain anonymous in any of Caitlin Cockerton's work.

CONSENT

I understand the purpose of this research and my questions have been answered. I have indicated whether my name, occupation and institutional affiliation can be written or whether I prefer to remain anonymous. I understand that I have the right to stop an interview at any time during the interview, and to withdraw permission to use part or all of the interview material within reasonable time after the conclusion of the interview.

I give my consent to participate in this research and be interviewed.

_____ _____ _____ _____
Participant's Signature Date Participant's Printed Name Date

_____ _____ _____ _____
Interviewer's Signature (witness) Date Interviewer's Printed Name Date

Contact details: Name: _____ Email: _____
Phone: _____

(iii) Further Agreement

This further agreement was made for the Cambridge iGEM advisors to further protect the participants. The agreement was signed and kept in my records. A similar agreement was made and signed by the leaders of the Imperial College iGEM team as well.

GOING SYNTHETIC: HOW SCIENTISTS AND ENGINEERS DREAM A NEW BIOLOGY INTO REALITY
Further discretionary agreement for
University of Cambridge participants
May 2009

In addition to the human subjects' consent form that will need to be completed by all participants in Caitlin Cockerton's research, this document provides a further discretionary agreement that aims to protect information of an individual personal nature of the involved iGEM participants. This document is to be signed by the researcher (Caitlin Cockerton) and co-ordinators of the 2009 Cambridge iGEM team.

Caitlin's research focuses on styles of thought and practices involved in iGEM and how these change over the course of the team's summer project. Broadly speaking, Caitlin seeks to understand how iGEMers imagine, design and construct a new synthetic biological entity. Although the research will involve exploring the thought processes and social dynamics that arise in a group of students from different disciplinary backgrounds, who are likely to have different approaches to their subject matter, Caitlin's work will maintain respect for the personal privacy of participants. Furthermore, as far as possible, Caitlin will try to avoid identifying features in presenting the interview data, but her work will disclose institutional affiliation and disciplinary background of involved iGEM participants. No iGEM student will be named by his or her real name; however, co-ordinators and other advisors or guest speakers involved with the iGEM team may or may not be named, as agreed to in individual consent forms.

Additional measures will be taken throughout the course of Caitlin's research in order to ensure that a suitable level of personal protection exists for participants:

- Caitlin has agreed NOT to blog her research in 'real time' and will seek approval of participants and the iGEM supervisors should she wish to make online postings related to this project. An exception may arise if it is deemed suitable that Caitlin contribute to the team's wiki site as the summer project develops.
- Interviewees have the right to stop participation in an interview or ask the researcher to have segments taken 'off-record'(within reasonable time after the conclusion of the interview).
- Caitlin will meet with iGEM supervisors periodically to discuss her research progress and come to an agreeable resolution to any potential conflicts of interest that may arise. Upon special request, coordinators of the iGEM team may access Caitlin's written material that draws upon data gathered in this research in order to assist in discussing and resolving such potential conflicts of interest.

It is taken in trust that, with the conditions stated, Caitlin can proceed with her research as a participant/observer with the Cambridge iGEM team of 2009.

Signed by:

- Caitlin Cockerton, Prof. X [Samuel], Prof. Y [Geoffrey] and Prof. Z [Frederick]

APPENDIX II

Intellectual Property / Open Source: supplementary excerpts

To provide the reader with a little further information from the BBF and the Registry, I have included the following excerpts from Endy and Grewal (2010).

(4.i) BBF is a not-for-profit organization that seeks to coordinate the creation of a repository of standardized synthetic biology elements and specifically meet the following goals:

- to develop and implement legal strategies to ensure that BioBrick™ standard biological parts remain freely available to the public;
- to support the development of open technical standards that define BioBrick™ standard biological parts, and;
- to develop and provide educational and scientific materials to allow the public to use and improve existing BioBrick™ standard biological parts, and contribute new BioBrick™ standard biological parts. http://bbf.openwetware.org/; http://bbf.openwetware.org/Our_Goals.html.

(4.ii) The BioBricks Legal Scheme (which shares obvious parallels to open software frameworks), proposed in January 2008, has the following three conditions:

> (1) You are free to modify, improve, and use all BioBrick™ parts, in systems with other BioBricks™ parts or non-BioBrick™ genetic material.
>
> (2) If you release a product, commercially or otherwise, that contains BioBrick™ parts or was produced using BioBrick™ parts, then you must make freely available the information about all BioBrick™ parts used in the product, or in producing the product, both for preexisting BioBrick™ parts and any new or improved BioBrick™ parts. You do not need to release information about any non-BioBrick™ material used in the system.
>
> (3) By using BioBrick™ parts, you agree to not encumber the use of BioBrick™ parts, individually or in combination, by others.[209]

(4.iii) There is currently a BioBrick™ Public Agreement (in Draft form, Version 1a) that is meant "[f]or public distribution and comment" (Endy and Grewal 2010). This working document shows how the BBF is working towards creating a mixed – open, yet also with patent provisions – IP framework for BioBrick™ parts (ibid). Currently, the document's preface reads:

> "The BioBricks Foundation, Inc. (the "Foundation") was established to foster and advance innovation, research, standardization, and education in synthetic biology through the open design, construction, distribution, understanding, and use of BioBrick™ compatible parts, namely standardized genetic materials and associated functional information, in ways that benefit the world. The Foundation believes that a free and easy-to-use legal framework for sharing and making use of engineered genetic materials underlies and serves these goals. Some such genetic materials may be subject to patents; some will not be. The patent-related provisions in this Contributor Agreement may or may not apply to the Materials" (ibid, 2).

Endy, D. and Grewal, D. (2010) *The BioBrick Public Agreement*, DRAFT Version 1a, January 2010:
http://dspace.mit.edu/bitstream/handle/1721.1/50999/BPA_draft_v1a.pdf?sequence=1

[209] http://openwetware.org/wiki/The_BioBricks_Foundation:Legal

APPENDIX III

(i) Imperial College 2009 iGEM team Human Practices project: supplementary document. This document was written by Andrew (and edited by me) to summarize the team's human practices work. It was disseminated via the team's Wiki and in hard-copy form at the Jamboree.

Imperial College 2009 iGEM team Human Practices project: supplementary documents..

Imperial College London 2009 iGEM Team
Human Practices Project

1. Why do human practices in iGEM?

Synthetic biology is clearly an exciting and inspiring area for those participating in iGEM. For the most part, our enthusiasm arises because we have got the chance to learn how to use the tools and techniques of synthetic biology in order to work towards applications that benefit humanity – with teams working towards more effective ways to deliver medicines, make biofuels, or even make bacteria smell nicer, the iGEM competition opens up a space for students to imagine how to make the world better, one BioBrick at a time. Yet, we believe that iGEM participants ought to go beyond learning about what synthetic biology can do and how to accomplish positive goals in this field.

It has become apparent in recent years that a number of social, political, legal and ethical issues circulate around synthetic biology (i.e. see Lentzos 2009). For example, there are concerns about how a sceptical public may perceive this technology as well as worries about biosafety, biosecurity and the fair distribution of knowledge and applications that disseminate from this field with mixed open source and IP regimes – and saying that merely scratches the surface!

As young iGEMers, a good number of us are likely to comprise the next generation of practicing synthetic biologists. It is therefore crucial that we enlarge our view to include an appreciation of this field's potential societal impacts. That is why we believe that iGEM students should think carefully about how we can help to develop this area of biotechnology in a safe and productive way, acknowledging and participating in discussions that address wider socio-political and ethical concerns. Such dialogue is already taking place at multiple levels – a number of scientists and engineers practising synthetic biology are participating in debate and discussion with public spheres, policy makers and social scientists in order to support development that aims at maximizing benefits and minimizing potential negative impacts of the field.

2. About our human practices project

Keeping in mind that a number of synthetic biologists are participating in the kind of dialogue discussed above, we thought it would be a good idea for us to get some practice at talking through the 'human practices' side of this field. That is why, with the help of Caitlin Cockerton (a PhD student from the BIOS Centre at London School of Economics), we developed a human practices project.

We decided to focus on three themes: (1) describing our work in easily understandable terms; (2) reflecting on the biological (some might even think 'life like') nature of the materials used in synthetic biology; and (3) addressing risks in our project and in synthetic biology in general. Caitlin conducted interviews with each of us in the iGEM team and these were recorded on video. This was where we had the chance to talk through our personal views on the three themes. We also participated in a group workshop with Caitlin, where we discussed and debated our views collectively. We have included a short video (see wiki) of some of our favourite clips from the interviews.

3. What we learned & suggestions for future iGEM human practices projects

From this enriching experience, we learned that such discussions are essential to the safe advancement of the field. Many of us expressed their desire to have a transparent scientific community where the scientists and society discuss freely about the expectations and risks that the field touches on. It was an interesting exercise to be pushed to articulate our views on topics that are indeed closely tied to our work in iGEM, but that sometimes we forget about when we are just 'doing the science and engineering'.

We need to be able to explain our work in understandable terms – this ties into the matter that synthetic biology will have to discuss and debate about this biotechnology in public spheres as the field progresses and begins to impact society.

We also ought to think about how others may perceive the manipulation and engineering of the components of life – although we may think biology can be 'black-boxed' and thought of in analogous ways to computer systems, others may disagree. It is for example important to keep in mind that the materials that are manipulated in synthetic biology do not have the same moral implications as existing, non-living technology such as the computer. It is important for us to appreciate that there will be many different views on what synthetic biology is about and we will need to create a framework within which all these different points of view can come together, discuss and shape the future of the field.

Finally – and this was something we knew right from the beginning of our project – it was essential that we all knew about how our project may be perceived as somewhat 'risky', in that the application would imply human beings could ingest capsules that are filled with proteins that have been made by a genetically engineered E. coli. We have built in strong safety measures into our project right from the beginning and we need to be able to articulate what this is about to others. We strongly believe that the wider sociological issues and concerns need to be addressed in the design of synthetic biological systems. This will show the commitment of the synthetic biologist towards the aim of creating a field that will contribute to the betterment of society as a whole.

In conclusion, we would recommend that future iGEM teams take on a human practices project of some sort. Even the simple exercise of reading and talking through some of the wider socio-political and ethical issues amongst fellow iGEM peers does a lot to benefit the field. If we begin now to work on developing ourselves as scientists and engineers who can relate our work to a bigger picture, it will only serve to benefit our research community and our society at later stages of synthetic biology's development.

Of course, there are many avenues to go down to take human practices projects further – do some public outreach by visiting schools or community centres to talk about synthetic biology; make questionnaires for members of the synthetic biology community or wider circles in our universities, cities or countries; think carefully about how to build in safeguards into our projects and then make sure we are able to talk about it clearly to lay audiences as well as to peers in the field. This is another reason why we are excited about coming together at the jamboree, as it is an ideal opportunity for discussion and debate around the aforementioned issues. We believe that as the next generation of synthetic biologists – and hopefully as the generation who will really be transferring the products of synthetic biology into society – it is essential for us to consider human practices of synthetic biology as an inherent part of our work!

Recommended reading…

For those interested in exploring literature more in the social sciences realm of synthetic biology (or biotechnology in general), the following reading list has been provided as a starting point… Happy reading!

(i) Some books and journals in the social sciences realm…

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Fox-Keller, E. (2009) 'What Does Synthetic Biology Have to Do with Biology?' *BioSocieties* Vol.4: 291-302

Hope, J. (2008) *Biobazaar: the Open Source Revolution and Biotechnology*, Cambridge, MA: Harvard University Press

Jasanoff, S. (2005) *Designs on nature: Science and Democracy in Europe and the United States*, Princeton, NJ: Princeton University Press

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(ii) Some links to interesting recent articles in popular intellectual media…

http://www.newyorker.com/reporting/2009/09/28/090928fa_fact_specter
http://www.economist.com/printedition/displaystory.cfm?story_id=14299634
http://www.wired.co.uk/wired-magazine/archive/2009/09/features/at-home-with-the-dna-hackers.aspx
http://www.nybooks.com/articles/20370

(iii) Articles in science journals address some of the wider social concerns surrounding synthetic biology too! See these for a start…

Bhattacharjee, Y. (2007) 'Gene-synthesis companies join forces to self-regulate,' *Science* Vol.316(22June): 1682

Bügl, H. et al. (2007) 'DNA synthesis and biological security,' *Nature Biotechnology* Vol.25(6): 627-9

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(ii) Imperial College 2009 iGEM team Human Practices project: supplementary document. This document was co-written by Andrew and his friend and was given out in hard copy at the Jamboree. (Note that the entire document is credited to these two students, so I have not added the references or made any editorial changes.)

Imperial College London
The E.Ncapsulator
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Synthetic biology and bioethics

The E.Ncapsulator project is a direct application of synthetic biology's theories. For that matter, it is important to analyze it from an ethical perspective: first of all, to make sure that the project is done according to the main principles of bioethics announced in the Belmont Report[210] and especially the principles of autonomy and beneficence. Moreover, it should also respect the idea of biosafety: genetically engineered products should not interfere with the environment – and especially with human health - to the point where it degrades it.

In addition of those basic ethical issues – that apply to other fields such as genetic engineering, synthetic biology raises moral and philosophical issues: does using DNA and genes, which are to some people the very core of life, as tools change the definition of life? Does it not blur our conceptions of what life is?

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I. The scientist and the layman

Synthetic biology is a new field. As such, its productions have not yet arrived in everyday life, nor has it changed it…yet. But already, many scientists talk about its potential; synthetic biology is seen by many as something that would change the world we live in. A European Commission report has tried to sum up all the fields synthetic biology could be used in and according to the report, applications could change the fields of medicine, pharmaceutical products, chemical industry, energy…[211]

Thus, it is fair to assume that synthetic biology will change our lives during the next decades, and that it will have an impact in reality itself.

Such promises create hopes, but fears as well: the same reluctance that exist in some countries towards GMO – whether they are legitimate or not – will come towards synthetic biology as soon as its products will be available to everyday life. We can even say that this reluctance will be more important, since some people already see synthetic biologists as God-playing scientists. As the European Commission Report puts it, "to some, this is sure to seem like 'playing God'"[212]. Therefore, it is important that scientists explain to the public what synthetic biology is, and explain both its risks and benefits.

We believe that the importance of taking human practices into account in the iGEM is to create awareness of this among young scientists. Not only is it important to be capable of explaining their project in lay terms, but also it is crucial that they fully understand why ethics are an important part of scientific life especially with regard to the link between science and society.

II. The E.Ncapsulator and biosafety

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[210] The Belmont Report
[211] The report of a NEST High-Level Expert Group (European Commission)
[212] Cf. supra, page 21.

One of the major themes in bioethics is the issue of biosafety. Ever since Dr. Eckard Wimmer announced that he and his team had artificially created the polio virus[213], fears were stirred among civil society. Incidentally, one of the main fears concerning synthetic biology is that a dangerous living organism could accidently – or even intentionally – escapes from a laboratory and cause a biological catastrophe. Perhaps it is that fear can be reduced to an over-reaction from people who don't know synthetic biology. As a matter of fact, most scientists will argue that the organisms used in laboratories would not resist a normal environment. However, asking for precaution from the synthetic biologists is a legitimate request. Thus, it falls naturally to ask that the International Biosafety Protocol[214] be applied in synthetic biology.

Being aware of such matters, the people working on the E.Ncapsulator project have decided from the beginning to use cells that could not hurt the environment and human health. Although some strains of Escherichia *coli* (commonly known as E.coli) can affect human health (e.g. Enterotoxigenic E. Coli), the strain used for the E.Ncapsulator (TOP10) was consciously chosen to be harmless. Thus, even if it did escape, however unlikely that event is, there would be no risk for the environment whatsoever: the E.Ncapsulator is biosafe.

Moreover, the E.Ncapsulator team is aware of what their project would look like to the eyes of people who do not know much about biology: eating an genetically engineered living pill can be repulsive for some people. In fact, not only can they fear a catastrophe, but they can also be reluctant to eating alive bacteria. For that reason, the E.Ncapsulator team added a module to their project. Module 3 is the genomic neutralisation of the bacteria – a phenomenon where the bacteria commit suicide by chopping up their DNA. That way, the team – assessing the public's potential fears – makes sure that these are minimized and the public reassured.

On a bioethical level, the E.Ncapsulator respects the notion of biosafety and also the principles of the Belmont Report. Indeed, its aim is to create genetically engineered pills aimed at curing or alleviating conditions such as Phenylketonuria. This project respects in full the principle of autonomy as it provides people with the choice of taking or not taking the pills. Furthermore, because those pills are meant to cure some malfunctions, it respects the principle of beneficence.

III. Moral and philosophical implications

Beyond those bioethical issues, synthetic biology raises moral and philosophical questions that do not seem to have been answered yet. For that matter, the E.Ncapsulator project is not an exception. Our goal here is not to give straight answers to all of these questions, but to raise awareness about some of them.

First of all, most philosophers until now tended to define morality in terms of ends and means. Immanuel Kant, founder of the modern conception of morality, thought that we should consider other people not as means to our ends, but as ends. When stealing from someone, a thief considers this person as the possessor of money you need, not as a full person whom you should respect. A good way to sum up morality would be : "Always recognize that individuals are ends, and do not use them as means to your end." [215] Some philosophers extended this principle to all living beings.[216] Synthetic biology uses life as a material – and therefore are not always considering what we could call "the sacred nature of life" – could be considered as immoral. On the other hand, so would a 16th century peasant building a house out of trees he cuts. This debate concerning synthetic biology and morality is certainly not the most important one, but it leads to a second philosophical –perhaps more important- question: how do we define life?

According to Edouard Machery, "a stable definition of 'life' is impossible and useless."[217] This *might* be true philosophically speaking, but one cannot deny the fact that synthetic biology will change the way people see life. For decades now, everyone has linked the vague concept of "life"

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[213] BBC News article from June 11th 2002
[214] Biosafety Protocol homepage
[215] Karl Popper, *The Open Society and Its Enemies* (1945)
[216] Hansson M.G, *Human Dignity and Animal Well-being: a Kantian Contribution to Biomedical Ethics* (1991)
[217] Quoted on page 27

to DNA and genes. Now however, the limit between life and objects becomes blurred, and we no longer have a scientific theory on which we can build our representation of what life is. *Life* is no longer in the genes, because the genes have become just another object we use in engineering. It is up to philosophers to redefine/recreate the concept of "life" – or at least to ease the acceptance of the fact that such a thing as *life* simply might not exist. As Shakespeare said, "Life every man holds dear"[218]. This might very well mean that by blurring the concept of "life", we are stealing "life" from ourselves –as human beings.

These issues are due to the very principles of synthetic biology. The E.Ncapsulator raises yet another issue: among the possibilities that this product offers is the delivery of cellulase in the intestine, an enzyme that breaks down cellulose to glucose. In theory, a cellulase capsule would allow people to eat... grass. Although, no precise definition of the human being exists, it does not usually cover grass-eating. One of the issues of synthetic biology is therefore this possibility of changing the human being and its very definition.

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The E.Ncapsulator project is bioethical: it respects core principles such as the principles of autonomy, beneficence, and biosafety. However it raises a number of philosophical issues. Even though these issues do not interfere with the scientists' every day work, the E.Ncapsulator team acknowledges them and believes scientists should participate in any future debates concerning the impact of synthetic biology on human conceptions of life or humanity.

[218] William Shakespeare, *Troilus and Cressida* (1602)