Synthetic Biology

Synthetic biology: constructing nature?

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Introduction

Synthetic biology is a new scientific field which literally aspires to construct nature, by building living things 'from scratch'. Because of this approach, it challenges our ideas about what we should think of as 'natural'. An important aspect of how we understand 'natural' rests on what we oppose it to (see Keller 2008a). In synthetic biology the main dichotomy is between the natural and the artificial. But other oppositions also become relevant: particularly those between the natural and the social, and the natural and the invented.

In what follows, I start with a brief description of synthetic biology and how it distinguishes itself from previous biotechnologies. I analyse the principles of an engineering approach to biology and show how these principles lead to aspirations amongst synthetic biologists to eliminate or reduce biological complexity in their synthetic creations. While some synthetic biologists want to 'improve' on nature (i.e. to make it easier to engineer), others want to replace certain natural phenomena with 'unnatural' alternatives. However, sceptics and critics argue that these blatant attempts to reduce complexity will not work, and that nature's contingency will not be successfully eliminated.

I then connect my discussion of synthetic biology to theoretical work by Paul Rabinow and Hans-Jörg Rheinberger on earlier biotechnologies, and discuss their analyses of the imposition of 'society' on 'nature' that we have seen in previous attempts to re-write and engineer biological systems.

I go on to contextualise our understanding of synthetic biology and its construction of nature by considering model organisms and intellectual property, both of which attempt to impose uniform properties on natural entities, and which have the potential to move their objects out of the realm of the natural and into the realm of the artificial.

In the conclusions I show how pressures for engineerability, commodification and standardization are all pulling in the same direction: towards a reconstruction of nature which is instrumentalizable and utilizable for our purposes. These pressures could have profound consequences for the kinds of living things that are brought into the world by synthetic biology.

This chapter draws on two years of research on the emerging field of synthetic biology. It is based on my experiences in being the social science member of a UK working party on synthetic biology, a founder member of a UK cross-university synthetic biology network, and my involvement in a synthetic biology 'sandpit'(which involved developing research proposals with synthetic biologists), as well as participation in numerous workshops, conferences and meetings in synthetic biology, from the largest conference in the field so far (Synthetic Biology 4.0 in Hong Kong in 2008), to meetings directed to young researchers and postgraduates (e.g. BioSysBio in

Cambridge 2009), to small discussion meetings internal to my own university and elsewhere. Detailed records have been kept throughout of my observations, conversations, interactions and reflections, so the empirical basis for this chapter is best described as a multi-sited ethnography (Marcus 1995). Synthetic biologists are only quoted here by name when I refer to a comment made in a public meeting; otherwise they are quoted by anonymised code name. I also draw on the burgeoning scientific literature in synthetic biology.

Synthetic biology

It is hard to provide a precise definition of any new and emerging scientific field, but defining synthetic biology is particularly difficult because it incorporates a number of disparate research activities under its banner. Broadly speaking, synthetic biology can be described as a field which aims to construct living systems *de novo*. The new kinds of biological entity it produces can be construed as being extremely unnatural and 'synthetic' – as the term 'synthetic biology' implies. Although 'synthesis' also has the meaning of synthesizing or putting together (i.e. the opposite of 'analysis'), it is the meaning of synthetic as 'artificial' which is the one that many commentators draw upon when discussing synthetic biology. In fact, attempts have been made to avoid the word 'synthetic' by naming the field 'constructive biology' or 'intentional biology' (Carlson 2006), but these names have not become widely adopted.

At the moment there is no consensus on the definition of the field. One of the most common definitions is a two-pronged one, which includes the construction of completely novel biological entities, and the re-design of already existing ones. For example, a group of leading scientists in the field defines synthetic biology as 'the design and construction of new biological parts, devices, and systems and the re-design of existing, natural biological systems for useful purposes'.[1]

Despite the lack of consensus, it is helpful to divide the disparate field of synthetic biology into three broad approaches (see O'Malley et al. 2008). The first approach, which is my main focus here, involves the building of interchangeable biological parts and devices called 'BioBricks' (see Endy 2005). The second approach covers work at the level of whole genomes, including both the synthesis of viral genomes from scratch (e.g. Cello et al. 2002) and attempts to strip away excess DNA from existing bacterial genomes, with the objective of producing the minimal genome necessary for life (Glass et al. 2006). The third approach centres on the creation of 'protocells' from simple components such as lipid vesicles (see Deamer 2005; Luisi et al. 2006).

An overriding principle which governs all three approaches is the attempt to engineer life, to such an extent that synthetic biology is called 'the engineer's approach to biology' (Breithaupt 2006). For example, the 'BioBricks' school, which is the dominant approach to synthetic biology, draws on the engineering principles of standardization, decoupling and abstraction with the objective of developing biological components which are interchangeable, functionally discrete and capable of being combined in a modular fashion, along the lines of 'plug and play' (Isaacs and Collins 2005, Brent 2004). These synthetic biologists hope that they will succeed in making biology into an engineering discipline where genetic 'engineering' failed (Breithaupt 2006; Endy 2005).

For this reason, synthetic biologists commonly distinguish their work from genetic engineering. There are two ways in which they do this. One is in terms of the

methods used. It is argued that since synthetic biology uses standardised parts and follows a formalised design process, the tools and intellectual approach of engineering are adopted in a way which makes synthetic biology more authentically like engineering. Another distinction is in terms of the 'sophistication' of the work. In genetic engineering one gene at a time is modified or added, whereas in synthetic biology a whole specialised metabolic unit can be constructed. This means that in synthetic biology we see engineering at the systems level, rather than at the level of the individual components. It should also be noted that another reason why synthetic biologists may be keen to distinguish their field from genetic engineering is because of some of the perceived negative social implications of genetic engineering.

The reason why synthetic biologists want to make biology into an engineering discipline is because they want to replicate the successes of engineering in a biological context. Synthetic biologists draw inspiration from the technological achievements of other branches of engineering, such as aircraft and computers, and conclude that it is "economically and socially important that we improve the efficiency, reliability and predictability of our biological designs" (Arkin 2008, p.774). Parallels are often drawn between today's synthetic biology and the early days of the nascent computer industry, with the intended implication that the technological revolution that synthetic biology brings will be as important as the revolution in ICTs brought about by electrical engineering (Barrett *et al*. 2006, NEST 2005).

As with other types of engineering, the range of applications of synthetic biology is potentially very broad, although the field is currently at an early stage of development. Examples of potential applications include microbial biofuel production (Keasling and Chou 2008), bioremediation, biosensors, new drug development pathways and synthetic vaccines (Royal Academy of Engineering 2009). Most notably, synthetic biology has successfully been used to produce a precursor for an antimalarial drug (Martin et al. 2003).

The reduction of complexity

While other emerging areas of biology (such as systems biology), embrace the complexity of biological systems, a key feature of the engineering approach to synthetic biology is the attempt to reduce biological complexity. Programmatic statements along these lines are common. For example, Heinemann and Panke (2006) say: 'As the complexity of existing biological systems is the major problem in implementing synthetic biology's engineering vision, it is desirable to reduce this complexity' (p.2793). Leading synthetic biologist Tom Knight also sees this aspiration to get rid of complexity as an integral part of the engineers' approach in maintaining that 'an alternative to understanding complexity is to get rid of it' (quoted in Ball 2004). One of the founders of synthetic biology, George Church, adopts a similar line: 'You focus on parts of the science that you do understand and clean out the parts that you don't understand' (quoted in Breithaupt 2006, p.22-3).

The approach we see here towards the complexity of nature is that it is better dispensed with, and that we will be more successful if we attempt to construct living systems from scratch without the unnecessary detritus that they have accumulated over evolutionary time. An example of this approach towards complexity is seen in the key paper 'Refactoring Bacteriophage T7' (Chan et al. 2005). The word 'refactoring' here is borrowed directly from computer software, and it means improving computer software by rationalising it and 'cleaning it up'.[2]

For some this reduction of complexity is not merely an instrumental aim, but is based on a faith that synthetic biology will ultimately lead to 'the elucidation of the underlying simplicity' of nature (Palsson 2000:1149). The pervasive idea of the simplicity of nature, and its connection to truth, is found throughout the history of biology (often in tension with ideas about its complexity – see Keller 2008b), and perhaps the most striking example of this is the iconic image of the double helix, famously described by Crick and Watson in 1953. Synthetic biologists draw inspiration from discoveries such as these and hope that the complexity of biological systems will be shown to be an eliminable accident of historical accumulations over evolutionary time (Balaram 2003).

Modularity in synthetic biology

A key requirement for the reduction of complexity is the assumption of modularity. Modularity is not a straightforward concept, but in engineering terms a module is defined as 'a functional unit that is capable of maintaining its intrinsic properties irrespective of what it is connected to' (Sauro 2008, p.1). Modular entities are very important in engineering because they can be extracted from one part of a system and inserted in another with no change in their function (Sauro 2008).

Modularity is crucial to the BioBricks school of synthetic biology where there is an on-line 'Registry of Standard Biological Parts'[3] which contains modular BioBricks that, in theory, can be connected to one another in a manner similar to pieces of lego (an analogy explicitly exploited by the Registry).

The issue of modularity is very interesting in the context of the discussion of nature. The key question here is whether biological systems are actually comprised of functional modules, or if they are simply best understood as such by the engineering approaches that are adopted in synthetic biology. There is no consensus on this issue. Arkin and Fletcher (2006) say that 'The key observation that biological systems exhibit some degree of modularity underlies the current belief that useful and 'engineerable' design principles exist' (p.2). And there are examples of entities that, at first glance, do appear to be modular and discrete, such as cells (Kitano 2002), ribosomes (Hartwell et al. 1999) and antibiotics (Synthetic biologist 5, November 15, 2008).

But there are others who see the idea of modularity as one that is imposed by the scientists and engineers involved. For example, even the proponents of abstraction hierarchies (the division of synthetic biology into parts, devices and systems that underlies the BioBricks approach) admit that these hierarchies are 'a human invention designed to assist people in engineering very complex systems by ignoring unnecessary details'.[4] We cannot necessarily deduce from this statement that these synthetic biologists think that modules are impositions of the engineer upon the biological substrate, but we can see a recognition that some aspects of synthetic biology are imposed on nature, rather than found within it. Other synthetic biologists argue that

modularity and standardisation in nature are myths, because biological function is always context dependent (Synthetic biologist 5, November 15, 2008).

Most synthetic biologists, however, do maintain that the modularity they aspire to find and build is present in biology, but even when agreement is reached on this issue, there is still a great deal of discussion over what constitutes a module, and whether this varies depending on the disciplinary perspective one adopts. The problem is that "modules mean different things to different specialists: the module of the developmental biologist is not the same as the module of the molecular geneticist" (Morange 2009, p.S50). Furthermore, biological entities have evolved to survive and not to be conveniently structured so that scientists can understand them (Keller 2008b). This means that what a cell regards as a functional module may be different from what a synthetic biologist regards as one (Oliver 2008). It may be that we are carving out modules in nature to fit our desires for biological understanding. Keller (2008b) warns that even if an assumption of modularity is helpful in the sense of enabling us to gain an understanding of biology (in an epistemological sense), we must be careful that we are not confusing epistemology with ontology.

There is also the point that all scientific knowledge must involve simplification and decontextualisation to an extent, in order to better focus on the subject of interest. As Barnes and Dupré (2008) note, in all attempts to gain knowledge some kind of reduction of complexity is perhaps inevitable: even perception involves reduction and simplification in order to prioritise the perceptual inputs that are most important.

But synthetic biology is particularly interesting in respect to modularity, because even if biology is not modular, perhaps synthetic biologists can make it so. The engineers' approach to eliminating annoying noise and crosstalk may result in an organism that is actually more modular than 'natural' organisms are. (This raises interesting questions about what such organisms might look like, and animals made of lego – one of the favourite analogies of the BioBricks school – spring to mind as a visual aid).

There is also the important point that attempts to break biological systems down into modular components not only makes biological complexity easier to deal with, but also makes these components more similar to software code which is modular, standardised and re-useable. One advantage of modularity is that several different researchers can work on different parts simultaneously, meaning that the field can develop faster. In this way, modularity is well-suited to open source principles, and many synthetic biologists are ideologically committed to open source, to such an extent that the aspiration to make their work open source is a guiding principle of the field.

Improving on nature

The idea of making living things more modular than they are 'naturally' gives rise to the potential of synthetic biology to improve upon nature. The idea underlying much synthetic biology is that making biological systems from scratch will make them better than they are in nature. Vitor Martins dos Santos (2008) describes synthetic biology along these lines as following three steps: understand the wiring, 'reprogram' and simplify. And the tag line which appears at the bottom of every page of the website of the BioBricks school is 'making life *better*, one part at a time'.[5]

It is pertinent here to ask what understanding of 'better' is being adopted in this tag line. From the perspective of a synthetic biologist, making life 'better' is making it easier to engineer. Here there is the potential for the imposition of engineering

principles on the form of living things, and arguably this is something that we are already starting to see. One of the main research objectives in synthetic biology has been to build analogues of engineering, such as oscillators and logic gates, in biological systems.[6] We see here the hope that synthetic biology will mimic the successes of electrical engineering, and it is it is telling that Hartwell et al. (1999) proclaim that 'The next generation of [biology] students should learn how to look for amplifiers and logic circuits' (p.C52). But these types of synthetic biological creations have been constructed on the basis of the assumptions that biological systems are modular and that feedback loops are important in explaining their operation. However, it has not been proven that these assumptions apply to 'natural' biological systems (Loettgers 2007).

Some of the more sceptical commentators see this approach as an imposition of the engineering mentality on natural systems, arguing that oscillators are rare in actual living systems (Synthetic biologist 6, 25th January 2008). Pottage and Sherman (2007) also make the point that 'the image of synthetic biology as an exercise in 'engineering' building blocks and programmable logic gates synthesised from inanimate materials, extends the mechanical and instrumental vision of nature into the deep texture of life' (p.545).

A good example of the way in which engineering principles are imposed by synthetic biology is found in one of the most important papers in the field which describes the building of a 'repressilator' (Elowitz and Leibler 2000), a genetic regulatory network that exhibits stable oscillation (although from an engineering point of view it is noisy and inflexible, Kitney 2008). What is interesting about the construction of the repressilator is that the aim of the work was not to reproduce experimental findings as accurately as possible. Instead, the researchers 'designed a network which would allow them to study not *natural* network designs but *possible* network design' (Loettgers 2007, p.141 emphasis added), so that they could learn more about how to develop alternative biological structures.

Although these synthetic networks may be functioning primarily as heuristic tools at the moment, in the process of doing synthetic biology these heuristic tools become material constructions. Again, there is the potential for the blurring of ontology and epistemology, because the reshaping of nature in synthetic biology is tied up with scientists' own epistemic practices.

Another rather audacious example of how epistemic practices can come to influence biological materiality is given by synthetic biologists who say that if they discover that their models of biological phenomena do not work, then they will simply engineer the biological parts to fit the model better (Synthetic biologist 8, 16th January 2009), rather than changing the model to make it a more accurate representation of the biological system, which is how biological research would have proceeded in the past.

A different kind of example of the imposition of engineering principles onto the natural world is the attempt to create a minimal 'chassis' into which biological functions can be slotted. The most cited example is the Venter Institute's work were scientists are attempting to strip away excess DNA from an existing microbial genome until they are left with the minimal genome which is necessary for life (Glass et al. 2006). Although the chassis school of synthetic biology is distinct from the BioBricks school, the aspiration is that the two will coincide in the future because the chassis will provide the substrate into which new BioBricks can be embedded.

It is worth reflecting on the metaphor of a 'chassis' here, and thinking about what work is being done with this familiar mechanical analogy: can we really think of

cells in these terms and consider slotting in different functional modules of DNA? The idea that it is possible to reduce 'life' down to its bare minimum, and then insert new functional parts into this minimum is a clear demonstration of an instrumentalist approach.

Changing nature

As well as attempts to make nature 'better' by stripping away unnecessary complexity, there are also attempts to make a biology that is different from that which is found in nature altogether. One of the objectives driving this work is to push the boundaries of natural systems and in this way learn more about them. Examples of this approach are Chin's work which involves producing amino acids from 4 instead of the normal 3 codons (see Chin 2008). An interest in the limitations of natural systems also drives research which attempts to develop new nucleic acids beyond the familiar As, Ts, Cs and Gs (Pollack 2001).

One motivation for this creation of 'unnatural' biological systems is to make modularity more successful. The idea here is that 'orthogonal' parts, could be designed, which perform the same function as their natural counterparts, but, because they are not naturally found in the cell, do not interfere with the existing cellular context and thus are more likely to be easily separable and manipulable (Weiss 2008).

This idea of orthogonal, alternative versions of natural systems is interestingly, and somewhat counter-intuitively, also used to argue for the safety of synthetic biological constructs. For example, it has been suggested that synthetic organisms could be made to be dependent on nutrients that are not found in nature (De Vriend 2006), or that they could have built-in safety features such as 'fail-fast' mechanisms (Endy 2005). One of the arguments made in favour of an alternative biological constructs is that we would not see 'interbreeding' between artificial and natural organisms (Lancet 2008). Here the assumption is that making synthetic organisms *less* natural will make them less risky, because they will be more easily separable from the natural world.

However, others point out that pushing the boundaries of natural systems in this way could lead to new and completely unexpected problems. Putting genes together that were previously separate could lead to the creation of new organisms that have unpredictable emergent properties (Tucker and Zilinskas 2006), making the risks of accidental release very difficult to assess in advance (De Vriend 2006).

Limitations to the reduction of complexity

The attempt to reduce complexity which underlies much of this work may not be achievable at all, however. The key question here is: 'Can the basic biological, evolutionary, non-linear aspects of living systems be engineered out?' (Rabinow in Lentzos 2008, p.315). Synthetic biologists are aware of these difficulties. For example, one says that the non-linearity of living systems makes them different from conventional engineering systems (Synthetic biologist 7, 5th Feb 2008), and Pam Silver describes a living organism as 'A long series of kludges…not necessarily a well-oiled machine' (Silver 2008). The philosopher William Wimsatt (2007) colourfully elaborates by saying we should think of 'Nature as a reconditioned parts dealer and crafty backwoods mechanic, constantly fixing and redesigning old machines and fashioning new ones out of whatever comes easily to hand' (p.10).

Synthetic biologists such as those in Ron Weiss' group in Princeton advise that 'it may be prudent to treat some biological uncertainties as fundamental properties of individual cell behavior' (Andrianantoandro *et al* 2006:13). They argue for a 'middle way'; acknowledging the complexity of biological systems but simultaneously not assuming that every single biological part is going to be a one-off. This leads Weiss to the conclusion that in synthetic biology it becomes important to think hard about 'what makes the biological substrate not like the other substrates we usually deal with' (Weiss 2008).

Others are more pessimistic and argue that we will see synthetic biology continually eluded in its quest to isolate the properties of living systems. The concern here is that by attempting to eliminate complexity and contingency, synthetic biologists might end up losing sight of the emergent properties that define living systems, which are themselves historical accumulations, being the result of billions of years of evolution (Balaram 2003 and Dupré forthcoming 2010). If this is correct we should not be optimistic about the attempts to construct life from modular and substitutable parts, which, in some guises, is the guiding objective of synthetic biology.

However, some commentators argue that those who point to the limitations of applying engineering principles to living systems are suffering from 'urea syndrome', i.e. they are assuming that there is something special and irreducible about living things and that it is by definition impossible to recreate them using scientific methods. This was the argument made about organic compounds before the successful synthesis of urea in 1828, which sent shockwaves through the scientific community of the time (Lazebnik 2002).

Nature modeled on culture

The previous discussion has shown how synthetic biology, like other biotechnologies that preceded it, works by 'extending the reach of human manufactures into the texture of life itself' (Pottage 2007, p.324). In this way, the attempts to manipulate and control nature that we see in synthetic biology are not new, and there are important continuities between synthetic biology and previous biological research. As Franklin (2006) says: 'The biologization of human values is in some ways as old as horticulture, when human preferences began to be nudged into seedlings, and mutated corn began to be selected for its ears' (p.179), but (to paraphrase her) this does not mean that synthetic biology does not have its own specificity. We could argue that what we see in synthetic biology is an extension of the potential of biotechnology, with improved capabilities for actually manipulating nature. It is not just that nature is being tamed, as it was with previous biologies. In synthetic biology nature is being explicitly remade.

The remodelling of the natural on the basis of an analogy with engineering that we see in synthetic biology is very similar to Rabinow's (1999[1992]) idea of 'biosociality', where, he says, 'nature will be modeled on culture' (p.411). He calls this 'biosociality' because he reverses 'socio-biology', where culture is 'constructed on the basis of a metaphor of nature' (p.411). This leads to an inversion of the temporal order in which we normally think about nature and culture, as Franklin (2000) explains: 'culture becomes the model for nature instead of being 'after nature', as if a kind of successor project' (p.194-5). A consequence of this is that 'biodiversity becomes a product of design choices, and industrial and political imperatives…rather than evolutionary pressures' (Allenby 2006).

Rabinow anticipates the developments in synthetic biology by saying that 'Nature will be known and remade through technique and will finally become artificial' (p.411). His work was written at the time of the sequencing of the human genome, and he predicts that what will be most interesting about the human genome is that it 'will be known in such a way that it can be *changed*' (p.408 emphasis added). The modification of nature has perhaps always been the objective of the biotechnological enterprise. But we could argue that this remaking, or re-writing, has only really become properly possible with synthetic biology.

Rheinberger (2000) traces the potential for changing nature back to the development of recombinant DNA techniques. He describes this development by saying that in early molecular biology there was an 'an extracellular representation of intracellular configurations' (p.19). In other words, the scientific objective was merely to represent what was going on inside the cell. But with the advent of recombinant DNA 'a radical change of perspective ensued. The momentum of gene technology is based on the prospects of an intracellular representation of extracellular projects – the potential 'rewriting' of life' (p.19). In this way ideas about what nature should be (i.e. extracellular, 'cultural' projects), could come to influence the intracellular environment. Rheinberger says that this potential for 'rewriting' makes molecular engineering 'substantially different from traditional intervention in the life sciences and medicine' because it involves '*re-programming* metabolic actions, not just interfering with them' (p.25). Rheinberger sees a technological potential here for intervening in a real sense, a potential which is being exploited by synthetic biology.

This leads Rheinberger to a very similar conclusion to Rabinow: 'the very essence of our being social is not to supersede, but to alter our natural, that is, in the present context, our genetic condition. We come to realise that the *natural* condition of our genetic makeup might turn into a *social* construct, with the result that the distinction between the 'natural' and the 'social' no longer makes good sense' (p.29).

Rheinberger makes heavy use of the metaphors of writing and programming, claiming that 'Within a timespan of less than twenty years, molecular geneticists have learned not only to understand the language of genes in principle, but to spell it' (p.24). Both these metaphors are ubiquitous in synthetic biology. For example, leaders of the field regularly talk about being able to 'write DNA' (Endy 2004). For this metaphor to have clout, DNA is assumed to take the form of information, which can be read (with the techniques of gene sequencing), and now written (using the techniques of synthesis) (Villalobos et al. 2006).[7] Many synthetic biology papers also talk about 're-programming' totally uncritically (Heinemann and Panke 2006, Dueber *et al* 2003, Gallivan 2007). To give an example, Gallivan (2007) says that 'One of the main goals of synthetic biology is to reprogram organisms to autonomously perform complex tasks'

(p.612). Slightly more reflection is found in a *Science* article which at least recognises that there is a gap between the organism and the computer programme in saying that 'Synthetic biologists eventually aim to make bacteria into tiny programmable computers.' (Ferber 2004, p.160).

Work by Rabinow and Rheinberger shows how culture and nature can be inverted, with 'cultural' frameworks (such as engineering and computation) having profound effects on the ways in which we construct living things. I hope to have demonstrated that these theoretical discussions help elucidate and enrich our understanding of synthetic biology.

Model organisms and intellectual property

Work in other areas can also contribute to an analysis of synthetic biology, and in this section I briefly discuss the attempts to standardise and control nature that we see in model organisms and intellectual property.

The modular biological parts that synthetic biologists are attempting to create have many similarities to the model organisms that have been standardized and homogenized so that they can be used reliably and predictably in laboratory work (Kohler 1999). For example, a key objective behind the development of the model worm *C. elegans* was 'reducing complex data to a conceptually and experimentally tractable system' (Ankeny 2000, p.S270). This is very reminiscent of the attempts to reduce complexity that we find in synthetic biology. In the case of the experimental mouse, the aim was to create mice which were so similar to each other that they were exchangeable, which is what we currently see in the development of modular BioBricks. We even see the use of the 'plug' metaphor in the mouse case:

> 'standardization is about what happens when one 'plugs in' a purified, specialized mouse into a research process (experiment, breeding program). If one such mouse is *substitutable* for another, then the mouse meets a standard of purity' (Griesemer and Gerson 2006, p.S366, italics in original).

The stabilization that we find in model organisms, which allows them to be useful laboratory tools, is also found in intellectual property, this time so that the living things can be easily exchanged in the market place (see Calvert 2008). For example, an argument made in favour of patenting microorganisms is that they 'are formed in such large numbers that any measurable quantity will possess *uniform properties and characteristics*.' (Judge Bastarache, Canada Supreme Court, 2002 in Dutfield 2008, p.3, emphasis added). If living organisms are uniform then they can be more easily treated as commodities.

A similar argument was made in the 1930 plant patent act. It was maintained that since asexually reproduced plants did not vary, they should be considered patentable (Pottage and Sherman 2007). Furthermore, the reproduction of a new plant of this kind could not be accomplished by nature, but had to involve human intervention. In this way the role of the breeder 'was to normalise the abnormal, to stabilise and standardise nature's deviants, mutations and aberrations' (Pottage and Sherman 2007, p.559). With this stabilization and standardization work, the buyer would know that they were getting a reliable product. This emphasis on standardisation and homogenisation, and the attempt to eliminate aberrations is again very reminiscent of synthetic biology. The catalogues that plant breeders produced so that their wares could

be bought as replicable copies (Pottage 2009) bear strong similarities to the 'catalog of parts and devices' that can be found on the BioBricks website.[8]

We see attempts to standardize in both model organisms and in intellectual property, but the two areas are linked in another way because model organism communities often share views about ownership. For example, the *Drosophila* community adopted strong norms of 'sharing and free exchange' (Kohler 1999:345), and *Drosophila* researchers are known for being particularly cooperative, even today. Similarly, the scientist who first produced the standardized experimental mouse did not aspire to profit from it, instead 'He favored traditional, cooperative exchange of materials as a service to the community of researchers' (Griesemer and Gerson 2006, p.366). The *C. elegans* community is also 'often celebrated as a model of scientific cooperation' (Ankeny 2000, p.S262). It seems as if model organism communities have accompanying norms which favour the sharing of their standardized organisms. Perhaps this sharing is necessary in a context where scientists are attempting to encourage buy-in to a particular standard.

We saw above how an open source approach was favoured by many synthetic biologists, and that modularity could be seen as facilitating such an approach. This is another demonstration of the similarities between synthetic biology and model organism communities, and in this light, it is interesting how at the closing session of the Synthetic Biology 4.0 conference in Hong Kong in 2008, explicit parallels were drawn between the synthetic biology community and the C. elegans community.

Another particularly important point about the model organism communities was how in the historical cases described above, the model organism, the social arrangements and the intellectual property norms were all produced together (Kohler 1999). In synthetic biology we also see explicit attempts among certain leaders of the field to build a community that shares a certain set of norms about open source (and also about biosafety), at the same time as we see the building of the BioBricks and the chassis that are the material building blocks of synthetic biology. This is a clear example of how natural and social orders are co-constructed (Jasanoff 2006). And in this example, as in many others in this volume, 'it is abundantly clear that technoscience and its artefacts are central to remaking society and nature simultaneously' (Braun and Castree 1998, p.29).

The open-source strand of synthetic biology is not the only one, however. There are also synthetic biologists who are keen to gain proprietary ownership over their synthetic creations.

As mentioned above, the 'unnaturalness' of synthetic organisms is used to argue for their safety, and their unnaturalness can also be useful in a patenting context, because it can be used to argue for their inventiveness. This is because the 'product of nature doctrine' holds that if something already exists in nature then it is not patentable, because it is not a novel invention. This doctrine can be traced back to the landmark Diamond versus Chakrabarty decision on a patent on a modified microorganism, where the court concluded that something could only be patented if it was 'a nonnaturally occurring manufacture or composition of matter – a product of human ingenuity' (447 US § 303 [1980], p. 309 in Conley and Makowski 2004). Since synthetic biology aims to de-complexify and improve on natural biological systems, its creations are clearly different from what is found in nature, so an argument can be made that they are human inventions, and that they deserve the reward of a patent.

Some synthetic biologists even purposely increase the unnaturalness of their creations, and make them more proprietary by marking them. Most notably, Craig Venter has 'watermarked' his name and the names of his collaborators into the code of his minimised bacterial genome, by inserting codons that produce proteins which correspond to the appropriate letters of the alphabet (Highfield 2008). This is a good example of a way in which synthetic biology plays with the boundary between the natural and the artificial, in the context of intellectual property.

There is a broader point here. Some commentators see the whole of intellectual property law as drawing on an entrenched distinction between the natural and the artificial. When something becomes intellectual property it is moved out of the realm of the natural into the realm of the artificial; it becomes an artefact (Biagioli 2007). But there are problems with presupposing that there is such a divide between the natural and the artificial, because it assumes that there is a stable concept of nature 'as such' – some kind of 'a pre-given substrate' (Pottage 1998). As we saw above, the arguments made by Rabinow and Rheinberger showed that culture can become a model for nature, making it very difficult to decide where culture ends and nature begins. Franklin points to exactly this problem when she says that

> 'The twentieth-century transformation of life itself has had the consequences that the grounding or foundational function of nature as a limit or force in itself has become problematic and lost its axiomatic, *a priori*, value as a referent or authority, becoming instead a receding horizon' (Franklin 2000, p.190).

Conclusions

This chapter has examined the ways in which synthetic biology is constructing nature. It is literally constructing nature by building new types of biological entity, but it is also constructing a new understanding of nature by challenging our notions of what is 'natural'. For example, we have seen how some synthetic biologists see themselves as improving on nature, while others emphasize the unnaturalness of their creations, to fit with patent demands or to produce orthogonal systems that do not interfere with existing biological contexts. However, although 'synthetic' is sometimes used as a synonym for 'artificial', it is unlikely that we will happily allocate all synthetic biological creations to the realm of the artificial. The standardized, modular, decomplexified creations of synthetic biology will inevitably start to infect our understandings of what is 'natural', which, as we have seen, is itself a 'receding horizon' defined primarily in terms of what it is opposed to.

I have argued that the objective behind the (re)construction of nature in synthetic biology is instrumental: the aim is to 'improve' on nature in order to make it easier to engineer. A key aspect of this improvement is the reduction of complexity, because 'the more dramatically researchers can reduce the complexity of biological organisms, the better they can turn these organisms into instrumentalizable media' (Pottage 2007, p.330). These tendencies may be a symptom of the 'instrumentalist epistemology of modern scientific culture overall' (Wynne 2005, p.77), which Wynne sees as driving research towards prediction and control and the potential for exploitation.

I have shown how synthetic biology is not exceptional in its attempts to instrumentalise nature, but that there are a confluence of different factors which all push in the same direction, and which include engineering, modularity, scientific practices,

model organisms, standardization, exchangeability, intellectual property, and even open source.

But we have also seen how the desire for prediction and control may be thwarted, and how there is a tension between the standardization which synthetic biologists attempt to impose on the biological substrate, and nature's apparent unruliness. Even in an 'age of biological control' (Wilmut et al. 2000), we see the non-cooperation of nature. A key objective of synthetic biology is to overcome this recalcitrance, which is why it is common to hear leading synthetic biologists talk of 'mastering nature' (Silver 2009), and of wanting to 'manipulate biology to give us the kind of things we want and not accept what nature gave us' (Keasling 2009). It will be fascinating to see how this tension will resolve itself in the context of synthetic biology, and what limitations the exuberance of nature will impose on the scientists and engineers' desires for control.

I will end by suggesting that that the example of synthetic biology can give us some very interesting insights into how 'the world 'outside' the laboratory comes to mirror the world inside' (Braun and Castree 1998, p.27). For example, we have seen how the epistemic ideal of modularity is imposed on the materiality of living things, and how synthetic biologists prefer to change nature than change their models, if they discover their models do not work as predicted. This goes further than Hacking's (1992) observation that technoscience enacts worlds that are fit for its methods, because the powers of intervention in synthetic biology are potentially much greater than those of previous biotechnologies. In synthetic biology we are seeing a reconstruction of nature that is utilizable and instrumentalizable, and is a product of epistemic ideals and design choices. This reconstruction may have profound consequences for the types of living things that are brought into the world in the future.

References

Allenby, B (2006) 'Biology as cultural artifact' http://www.greenbiz.com/blog/2006/10/01/biology-cultural-artifact (accessed 30th May 2009)

Andrianantoandro E, Basu S, Karig DK, and Weiss, R (2006) 'Synthetic biology: new engineering rules for an emerging discipline' *Molecular Systems Biology*, doi: 10.1038/ msb4100073

Ankeny, RA (2000) 'Fashioning Descriptive Models in Biology: Of Worms and Wiring Diagrams' *Philosophy of Science*, Vol. 67, Supplement. Proceedings of the 1998 Biennial Meetings of the Philosophy of Science Association. Part II: Symposia Papers, (Sep., 2000), pp. S260-S272

Arkin, A (2008) 'Setting the standard in synthetic biology' *Nature Biotechnology*, 26, 7: 771-774

Arkin AP, Fletcher DA. (2006) 'Fast, cheap and somewhat in control' *Genome Biol* 7:114

Balaram, P (2003) 'Synthesising life' *Current Science*, vol. 85, no. 11, 1509-1510

Ball, P (2004) 'Starting from scratch' *Nature* (7th October 2004), 431: 624-6.

Barnes, SB and Dupré, JA (2008) *Genomes and What to Make of Them*, University of Chicago Press

Barrett C.L., Kim T.Y., Kim H.U., Palsson B.Ø. and Lee, S.Y. (2006). Systems biology as a foundation for genome-scale synthetic biology. *Current Opinion in Biotechnology, 17*(5), 1-5

Biagioli, M (2007) 'Denaturalizing the public domain: How to use science studies to rethink IP', Talk at the University of Edinburgh, 10th December 2007

Braun, B and Castree, N (1998) *Remaking reality: nature at the millennium*. Routledge: London and New York

Breithaupt, H (2006) 'The Engineer's Approach to Biology' *EMBO Reports* 7 (1), 21-24

Brent, R (2004) 'A partnership between biology and engineering' *Nature Biotechnology*, 22(10), 1211-1214

Calvert, J (2008) 'The commodification of emergence: systems biology, synthetic biology and intellectual property' *BioSocieties* 3(4): 385-400

Carlson, R (2006) Synthetic biology 2.0, Part IV: What's in a name? http://synthesis.typepad.com/synthesis/2006/05/synthetic_biolo_1.html (accessed 1st December 2008)

Cello J, Paul AV, Wimmer E. (2002) 'Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template' *Science* 297: 1016-1018

Chan LY, Kosuri S, Endy D (2005) 'Refactoring bacteriophage T7' *Mol Sys Biol* DOI: 10.1038/msb4100025.

Chin, J (2008) 'Life and perpetuation of life of a synthetic bacterium' EMBL/EMBO Science and Society Conference, Heidelberg, Germany, 7th-8th November 2008

Conley, JM and Makowski, R (2004) 'Rethinking the product of nature doctrine as a barrier to biotechnology patents in the United States – and perhaps Europe as well ', *Information & Communications Technology Law*, 13:1, 3-40

Deamer D. (2005) 'A giant step towards artificial life?' *Trends in Biotechnology* 23:336–338

Dupré, J (forthcoming 2010) 'Is it not possible to reduce biological explanations to explanations in chemistry and/or physics' in Francisco Ayala and Robert Arp (eds) *Contemporary Debates in Philosophy of Biology* Wiley

Dueber, JE, Yeh, BJ, Chak, K, Lim, WA (2003) 'Reprogramming control of an allosteric signaling switch through modular recombination' *Science* 301, 1904–1908

Dutfield, G (2008) 'Who invents life - intelligent designers, blind watchmakers, or genetic engineers?' SIBLE Seminar Series, University of Sheffield, 5 March 2008

Elowitz, MB and Leibler, S (2000) 'A Synthetic Oscillatory Network of Transcriptional Regulators' *Nature*. Jan 20; 403(6767):335-8

Endy, D (2004) 'Parts, devices & systems: engineering biology at MIT' Synthetic Biology 1.0, MIT, 10th-12th June 2004

Endy, D (2005) 'Foundations for Engineering Biology' *Nature* 438 (24 November 2005), 449-453

Ferber, D (2004) 'Microbes made to order' *Science*, 303 (9 January 2004), 158-161

Franklin, S (2000) 'Life Itself: Global Nature and the Genetic Imaginary', pp. 188-227 in Franklin, S Lury, C and Stacey, J *Global Nature, Global Culture*. London: Sage
Franklin, S (2003) 'Kinship, genes, and cloning: Life after Dolly' in A Goodman, D Heath, & S Lindee (eds), *Genetic Nature/Culture: Anthropology and Science Beyond the Two-Culture Divide*, 95–110. Berkeley: University of California Press.
Franklin, S (2006) 'The Cyborg Embryo: Our Path to Transbiology' *Theory, Culture and Society* 23; 167-187
Gallivan, JP (2007) 'Toward reprogramming bacteria with small molecules and RNA' *Curr Opin Chem Biol*. 2007 December; 11(6): 612–619.
Glass, JI., Assad-Garcia, N, Alperovich, N, Yooseph, S, Lewis, MR, Ma-ruf, M, Hutchison III, CA., Smith, HO., and Venter, JC (2006) 'Essential Genes of a Minimal Bacterium' *Proc Nat Acad Sci* 103 (2), 425-430.
Griesemer, JR and Gerson, EM 'Essay review. Of mice and men and low unit cost' (review of Making mice: Standardizing animals for American biomedical research, 1900–1955. Karen A. Rader; Princeton University Press, Princeton, NJ, 2004)' *Stud. Hist. Phil. Biol. & Biomed. Sci.* 37 (2006) 363–372
Hacking, I, (1992) 'The Self-Vindication of the Laboratory Sciences', pages 29–64 in Pickering, A., (ed.), *Science as Practice and Culture*, Chicago and London: Chicago University Press
Hartwell LH, Hopfield JJ, Leibler S, Murray AW. (1999) 'From molecular to modular cell biology' *Nature* 402, C47–C52
Heinemann M and Panke, S (2006) 'Synthetic biology – putting engineering into biology' *Bioinformatics*, 22(22), 2790-2799
Highfield, R (2008) ''Watermarks' written in first artificial genome' *Telegraph*, 01 Feb 2008
Isaacs, FJ and Collins, JJ (2005) 'Plug and play with RNA' *Nature Biotechnology*, 23(3), 306-307
Jasanoff, S (2006) *States of Knowledge: The Co-Production of Science and the Social Order*. New York: Routledge
Keasling, J (2009) 'Keynote lecture' Launch Event for the Centre of Synthetic Biology at Imperial College, 12th May 2009
Keasling, JD and Chou, H (2008) 'Metabolic engineering delivers next-generation biofuels' *Nature Biotechnology* 26, 298 - 299
Keller, EF (2008a) 'Lecture: nature and the natural' *BioSocieties*, 3, 117–124
Keller, EF (2008b) 'Systems biology: new paradigm or just fashion' EMBL/EMBO Science and Society Conference, Heidelberg, Germany, 7th-8th November 2008
Kevles, DJ (2002) *A History of Patenting Life in the United States with Comparative Attention to Europe and Canada* A report to the European Group on Ethics in Science and New Technologies, 12th Jan 2002 Luxembourg: Office for Official Publications of the European Communities
Kitano, H (2002) 'Computational systems biology' *Nature*, 420, 14th November 2002, 206-210
Kitney, R (2008) 'Overview of Design Principles' Synthetic Biology 4.0, Hong Kong, 10th-12th October 2008
Kohler, RE (1999) 'Moral economy, material culture, and community in *Drosophila* genetics' in Biagioli, M ed, *The Science Studies Reader* New York: Routledge
Lancet, D (2008) 'Diversity: a driving force for life's inception and synthesis' EMBL/EMBO Science and Society Conference, Heidelberg, Germany, 7th-8th November 2008
Lazebnik, Y (2002) 'Can a biologist fix a radio?—Or, what I learned while studying apoptosis' *Cancer Cell* vol. 2, pp.179-182
Lentzos, F, Bennet, G, Boeke, J, Endy, D and Rabinow, P (2008) 'Roundtable on synthetic biology: visions and challenges in redesigning life' *BioSocieties* 3, 311-323
Luisi PL, Ferri F, Pasquale, S (2006) 'Approaches to Semi-synthetic Minimal Cells: A Review' Naturwissenschaften 93 (1), 1–13
Loettgers, A (2007) 'Model Organisms and Mathematical and Synthetic Models to Explore Gene Regulation Mechanisms' *Biological Theory* Spring 2007, Vol. 2, No. 2, 134-142

Martin VJJ, Pitera DJ, Withers ST, Newman JD, Keasling JD. (2003) 'Engineering a mevalonate pathway in Escherichia coli for production of terpenoids' *Nature Biotechnology* 21:796–802
Martins dos Santos, V (2008) 'Powering Cell Factories' Synthetic Biology 4.0, Hong Kong, 10th-12th October 2008
Marcus, GE (1995) 'Ethnography in/of the World System: The Emergence of Multi-Sited Ethnography' *Annual Review of Anthropology* Vol. 24: 95-117
Morange, M (2009) 'A new revolution? The place of systems biology and synthetic biology in the history of biology' *EMBO reports*, vol. 10, pp.S50-S53
NEST (2005) *Synthetic Biology: Applying Engineering to Biology* Report of a NEST High-Level Expert Group Luxembourg: Office for Official Publications of the European Communities online at
ftp://ftp.cordis.europa.eu/pub/nest/docs/syntheticbiology_b5_eur21796_en.pdf (accessed 14th September 2008)
Oliver, S (2008) 'Synthetic and Systems Biology: Simplicity and Simplification' Discussion Meeting on Synthetic Biology, Royal Society, London, 2nd-3rd June 2008
O'Malley, MA, Powell, A Davies, JF, and Calvert, J (2008) 'Knowledge-making distinctions in synthetic biology' *BioEssays*, 30 (1), 57-65
Palsson, B (2000) 'The challenges of in silico biology' *Nature Biotechnology* Vol 18 November 2000, pp.1147-1150
Pollack, A (2001) 'Scientists Are Starting to Add Letters to Life's Alphabet' *New York Times*, 24 July 2001
Pottage, A (1998) 'The inscription of life in law: genes, patents, and bio-politics' *Modern Law Review* 61: 740-65
Pottage, A (2007) 'The socio-legal implication of the new biotechnologies' *Annual Review of Law and Social Science* 3:321-44
Pottage, A (2009) 'La mécanisation propriétaire du vivant' La co-définition du vivant et des droits de propriété, Paris, 9 April 2009
Pottage A and Sherman, B (2007) 'Organisms and manufactures: on the history of plant inventions' *Melbourne University Law Review*, 31(2), 539-568
Rabinow, P (1999 [1992]) 'Artificiality and Enlightenment: From Sociobiology to Biosociality' in Biagioli, ed., *The Science Studies Reader* (Routledge), pp 407-416.
Rheinberger, H-J (2000) 'Beyond Nature and Culture: Modes of Reasoning in the Age of Molecular Biology and Medicine', in M. Lock, A. Young and A. Cambrosio (eds) *Living and Working with the New Medical Technologies: Intersection of Inquiry*, pp. 19–30. Cambridge: Cambridge University Press
Royal Academy of Engineering (2009) *Synthetic Biology: Scope, Applications and Implications* Royal Academy of Engineering: London, May 2009 online at
http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf (accessed 5th July 2009)
Sauro, HM (2008) 'Modularity Defined' *Molecular Systems Biology* 4:166
Silver, P (2008) 'Designing Biological Systems' Discussion Meeting on Synthetic Biology, Royal Society, London, 2nd-3rd June 2008
Silver, P (2009) 'Design Principles in Biological Systems' Launch Event for the Centre of Synthetic Biology at Imperial College, 12th May 2009
Tucker JB, Zilinskas RA. (2006) 'The promise and perils of synthetic biology' *New Atlantis* 12: 25-45
Villalobos , A, Ness, JE, Gustafsson, C, Minshull, J and Govindarajan, S (2006) 'Gene Designer: a synthetic biology tool for constructing artificial DNA segments' *BMC Bioinformatics* 7:285 doi:10.1186/1471-2105-7-285
De Vriend, H (2006) *Constructing Life. Early social reflections on the emerging field of synthetic biology*. The Hague: Rathenau Institute; Working Document 97 online at
http://www.rathenauinstituut.com//showpage.asp?steID=2&item=2644 (accessed 25th February 2008)

Weiss, R (2008) 'The iGEM Undergraduate Competition' Synthetic Biology 40, Hong Kong, 10th-12th October 2008
Wimsatt, W (2007) *Re-engineering philosophy for limited beings: piecewise approximations to reality* Cambridge, Massachusetts: Harvard University Press
Wilmut, I, Campbell, K and Tudge, C (2000) *The Second Creation: The Age of Biological Control by the Scientists Who Cloned Dolly* London: Headline
Wynne, B (2005) 'Reflexing complexity: post-genomic knowledge and reductionist returns in public science' *Theory, Culture and Society*, 22(5), 67-94

[1] www.syntheticbiology.org (Accessed 30th April 2010)
[2] http://www.refactoring.com/
[3] http://partsregistry.org/Main_Page/ (Accessed 30th April 2010)
[4] http://www.openwetware.org/wiki/Synthetic_Biology:Abstraction_hierarchy (Accessed 30th April 2010)
[5] www.syntheticbiology.org (emphasis added) (Accessed 30th April 2010)
[6] Oscillators and logic gates are common components of electronic circuits. An oscillator produces a repetitive electronic signal and a logic gate switches the flow of electricity 'on' or 'off' depending on the input.
[7] For criticism of this understanding of DNA as informational see Barnes and Dupré (2008).
[8] http://partsregistry.org/Main_Page (Accessed 30th April 2010)