Original Article

Ownership and sharing in synthetic biology: A 'diverse ecology' of the open and the proprietary?

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Abstract Synthetic biology is in the process of inventing itself and its ownership regimes. There are currently two dominant approaches to ownership and sharing in the field. The work of the J. Craig Venter Institute is grounded in molecular biology and in gene patenting. Parts-based approaches to synthetic biology, in contrast, are inspired by engineering, open source software and distributed innovation, and they are building new communities to help further this agenda. Despite these differences, the two approaches make very similar use of informational and computational metaphors. They both also have a place in a vision for the future of synthetic biology as a 'diverse ecology' of the open and the proprietary. It remains to be seen whether such a diverse ecology will be sustainable, whether synthetic biology will go down the patenting route taken by previous biotechnologies or whether different forms of ownership and sharing will emerge. Which path is taken will depend on the success of synthetic biology in achieving both its technical objectives and its social innovations.

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Introduction

A cursory look at the field of synthetic biology reveals two dominant approaches to intellectual property (IP). On the one hand, there is the work of the J. Craig Venter Institute (JCVI), which is grounded in molecular biology, and has a long tradition of filing patents. On the other, there are engineering-oriented parts-based approaches to synthetic biology, which draw their inspiration from open source software. In this article, I show how the IP approach of the JCVI can be seen as a continuation of gene patenting, whereas parts-based synthetic biology draws on a different tradition of distributed innovation. Crudely put, the contrast is between the proprietary and the open, although, as we will see, the situation is in reality more complicated.

There are other approaches to synthetic biology of course (see O'Malley *et al*, 2008), stretching from the creation of alternative genetic alphabets (Pollack, 2001) to attempts

to recreate the conditions under which life originated in the universe (Luisi *et al*, 2006). However, the two approaches I focus on here have the most relevance for IP debates. It is significant that they both also make particularly striking use of informational and computational metaphors. For example, Venter talks about 'booting up' a cell with a synthetic genome, and proponents of parts-based approaches emphasise the inter-convertability of genetic information and material, enabled by DNA sequencing and synthesis technologies. The same metaphors are used for very different purposes, however. Whereas the JCVI uses them to extend their proprietary claims, parts-based approaches engage in explicit attempts to introduce norms of openness and sharing into the field.

It is important not to overemphasise the differences between these two approaches, however, as both have to grapple with context-dependent and recalcitrant biological systems. Furthermore, the attempt to develop a bespoke ownership regime for standard biological parts explicitly aims to foster a 'diverse ecology' of the open and the proprietary.

This article draws on 5 years of engagement with the emerging field of synthetic biology as a participant observer in a range of different sites in Europe and the United States, including attendance at numerous workshops, conferences and meetings. I also draw on the scientific literature in synthetic biology, as well as policy reports and grey literature. The extent to which social scientists studying synthetic biology can (or should) think of themselves as part of the synthetic biology community is an important methodological question, but one that extends beyond the scope of this article.[1]

Gene Patenting

It is helpful to ground a discussion of IP in synthetic biology in the much longer running practice of gene patenting. There is a wealth of literature on gene patenting that I will not rehearse here.[2] For the purposes of this article, what is particularly interesting is how genes came to be thought of as carriers of information in patent contexts. Kay (2000) shows how the introduction of informational metaphors such as the 'genetic code' into the biological sciences should be understood as part of a broader shift to informational thinking in many fields in the late 1940s and early 1950s. Informational metaphors became extremely influential in molecular genetics, which blossomed after the discovery of DNA in 1953 (Keller, 2000; Moss, 2003). Dupré (2004) argues that molecular genetics changed the representation of the gene from 'Mendelian' to 'molecular'. A Mendelian gene can be understood as a hypothetical factor that is statistically correlated with a phenotypic trait. A molecular gene, in contrast, is usually described as a specific stretch of DNA that codes for a particular polypeptide. What is important about the move from Mendelian to molecular genes is that it not only transformed a gene into a material entity, but also into a carrier of information (Rheinberger, 2000).

This material/informational duality of the gene was sidestepped in patent law, however, because when genes first started being patented in the late 1970s and early 1980s they were simply treated as if they were chemical compounds. By this time, 'isolated and purified'

1 I explore this issue in Calvert (forthcoming).
2 See, for example, Conley and Makowski (2003) and Demaine and Fellmeth (2002).

naturally occurring chemical compounds could be patented, as long as they fulfiled the other requirements for patentability (Demaine and Fellmeth, 2002; Conley and Makowski, 2003), thus this argument was simply extended to genes, and it led to a proliferation of patenting activity around genetic entities (Nuffield Council on Bioethics, 2002).

One infamous example of such activity was an attempt by the US National Institutes of Health, led by Craig Venter, to patent thousands of short DNA sequences called 'Expressed Sequence Tags' (or ESTs) in 1991–1992. The patent applicants knew that these DNA sequences were expressed, and surmised that they played an important biological role, but they did not know what this role was (Cornish *et al*, 2003). This attempt to patent ESTs was ultimately unsuccessful, but it is important because it shows the limitations of treating genes as chemical compounds. The reason that the ESTs were considered potentially valuable was not because of their chemical nature, but because of their potential role as carriers of information (Rai, 1999).

It is well known that Venter was at the centre of the attempt to patent ESTs, but he was also behind some other important patents in the 1990s, which usually receive much less attention, although they are particularly relevant to recent proprietary moves in synthetic biology.

In the 1990s, the Institute for Genomic Research (now part of the JCVI) sequenced the genomes of the scientifically important bacteria *Haemophilus influenzae* (Fleischmann *et al*, 1995) and *Mycoplasma genitalium* (Fraser *et al*, 1995) and the Archaea *Methanococcus jannaschii* (Bult *et al*, 1996). In each case, a patent was filed on the genome sequence before its publication by the affiliated company Human Genome Sciences (Shreeve, 2004; O'Malley *et al*, 2005). What is interesting about these patent applications is that, like the earlier ESTs applications, they were based on the informational properties of the DNA sequences. These applications went further than the ESTs applications, however, because all three of them originally claimed the complete genome sequence in 'computer-readable medium'. The patent specifications argued that having the genome sequences in such a form would allow them to be used in comparative searches against existing DNA databases, and that this would help identify parts of the genome with commercial or biological significance. The three applications did not survive the examination procedure in this form, however. When they were finally granted, the patents claimed specific DNA sequences in a more conventional manner (Bostanci and Calvert, 2008).

These applications should be understood in their historical context, where computation and bioinformatics were becoming increasingly important in molecular biology (Cook-Deegan, 1994). Computer software was also becoming patentable in the mid-1990s in the United States, thanks to a series of court rulings (Bonaccorsi *et al*, 2011). Although the computer-embodied genome patents were ultimately not successful, they are an indication of an informational shift in genomics and patenting that was happening at the time. The emphasis on the informational importance attributed to the genome is shown by the fact that in the original patent applications, the genomes were referred to as the 'life sustaining instructions and information' of the organism.[3] This particular understanding of the role of the genome is central to synthetic biology, but it has been heavily critiqued by philosophers, scientists and other commentators (see, for example, Sarkar, 1996; Kay, 2000; Keller, 2000;

3 USPTO Applications Nos. 08/476,102 and 08/545,528.

Moss, 2003; Barnes and Dupré, 2008). This literature argues that the phenotypic properties of an organism cannot be reduced to the properties of its genes, because an organismal properties are context-dependent and emerge at higher levels of organisation.

Patent law avoided these discussions, however, by persisting in treating genes as if they were merely chemical compounds, until recent developments re-invigorated the debate (Calvert and Joly, 2011). In April 2010, the patent world was shocked by Judge Sweet's ruling at the United States District Court for the Southern District of New York, which invalidated patents owned by the company Myriad Genetics that test for breast cancer susceptibility genes (Association for Molecular Pathology *et al* v. USPTO *et al*, 2010). The ruling is based on exactly the same argument made by Rheinberger (2000) above, that genes are both informational and material:

> Genes are of double nature: on the one hand, they are chemical substances or molecules. On the other hand, they are physical carriers of information, i.e., where the actual function of this information is coding for proteins. (Association for Molecular Pathology *et al* v. USPTO *et al*, 2010, p. 7)

The decision goes on to argue that this informational quality is unique among chemical compounds, and that as this quality is the same for the gene in isolated and purified form as it is in nature, genes constitute unpatentable subject matter. This decision has been appealed and may be reversed,[4] but what I want to draw attention to here are the divergent conclusions that can be drawn from the notion that genes are 'the physical embodiment of biological information' (Association for Molecular Pathology *et al* v. USPTO *et al*, 2010, p. 3). As noted above, this type of genetic reductionism is heavily critiqued for ignoring the contingency and context-specificity of the operation of a gene, but, in this case, it is precisely because the genetic information is regarded as 'the same' in two very different contexts (in the body and in the genetic test) that Judge Sweet was able to make the argument that the gene should not be patented. Here we see genetic reductionism being used to argue against gene patenting.

Synthetic Genomes

A very similar notion of the informational nature of DNA is found in the JCVI's recent paper 'Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome' (Gibson *et al*, 2010). This article was heralded as a landmark achievement because an entirely synthetic version of a natural genome was created and implanted into a recipient cell, where it took over the function of that cell and successfully replicated. The scientists named the synthesised version of the natural *Mycoplasma mycoides* bacteria '*Mycoplasma mycoides* JCVI-syn1.0' (note the use of the software naming convention). In describing this work, Venter talked about how the synthetic genome 'booted up' the recipient cell (Sample, 2010).

4 In fact, this decision was overruled in July 2011 in the Court of Appeals for the Federal Circuit (CAFC). Interestingly, the idea that DNA is chemical (rather than informational) and that it can be reduced to its chemical nature was assumed by one of the CAFC judges, who argued that merely detaching a segment of DNA from its natural context gives it a different chemical identity. The American Civil Liberties Union will be pursuing Myriad in the Supreme Court (Allsup, 2011).

He also said that this was 'the first cell to have its parent be a computer' (Jones, 2010), meaning that the sequence was determined in a computer before being synthesised in material form. The published scientific article reinforces these notions by saying that 'DNA sequencing of a cellular genome allows storage of the *genetic instructions for life* as a digital file' (Gibson *et al*, 2010, p. 4, emphasis added). In addition, the authors continue this computational metaphor by adding that 'the DNA software builds its own hardware' (ibid.).

Although this article received a large amount of media attention, it was a proof-of-principle experiment, with the longer-term aim of developing a simplified synthetic minimal genome, with all non-essential genes deleted. This is where Venter's earlier work, discussed above, becomes relevant. One of the genomes that The Institute for Genomic Research chose to sequence (and patent) in the mid-1990s was the bacteria *Mycoplasma genitalium*. This organism was chosen because it has one of the smallest known natural genomes, being an obligate parasite, which is dependent on its host for many essential nutrients. It provided the ideal starting point for work on constructing a streamlined, minimal genome.

Venter is notorious for vigorously pursuing IP rights, as demonstrated by the ESTs episode described above, thus it is not surprising that his group has already filed several patents relating to this recent work. The most controversial is an application filed in May 2007 for the smallest genome needed for a living organism (Glass *et al*, 2007).[5] The patent application, simply entitled 'Minimal bacterial genome', starts its first claim with 'A set of protein-coding genes that provides *the information required* for growth and replication of a free living organism …' (emphasis added). In this patent application, as in previous whole genome applications from this group, as well as in their recent paper, we see again the idea that genes provide the crucial 'instructions for life'. In contrast to the Myriad case, however, this understanding of genes is used to argue that they are the legitimate target of patent applications.

The group hopes that its simplified cellular 'chassis' will be used to build new life forms that perform useful functions (such as develop biofuels), and it is for this reason that the patent application specifically claims the use of the minimal cell for hydrogen or ethanol production. This has led some groups to worry that such claims could potentially lead to the dominance of one particular chassis, allowing the Venter Institute to become the 'Microbesoft' of synthetic biology (ETC Group, 2007). However, we should not forget that this patent is still at the application stage, and many commentators think it has little chance of being granted (Nature Biotechnology, 2007).

The attempt to assert ownership over biological entities is of course not unique to the JCVI, or to synthetic biology, but it is part of a much broader movement to transform living substances into marketable products, a movement that has been the focus of recent literature on 'biocapital' (see, for example, Rose, 2006; Sunder Rajan, 2006; Helmreich, 2008). This work shows how developments in the biosciences have allowed things such as microbes, cells and genes to become commodities (Rahaman, 2011). For something to be a commodity it must be mobile, and detachable from its original context (Callon, 1998). Rose (2007) describes this as a 'flattened' world, where 'almost any vital element can, in principle, be

5 Other important method applications that I do not have space to discuss here are Venter *et al* (2007) 'Synthetic genomes' (application number 11/635,355, filed in 2006), and Gibson *et al* (2009) 'Assembly of large nucleic acids' (application number 12/247,126, filed in 2008).

freed from its ties to cell, organ, organism, or species, set free to circulate and to be combined with any other' (p. 16). It is only when the world is 'flattened' in this way that biological entities emerge as things that can be owned. These arguments resonate with the literature discussed above that is critical of genetic reductionism, which suggests that this flattened world provides an impoverished understanding of living things.

Bearing this in mind, it is notable that the striking genetic reductionism of both the 2007 minimal genome patent application and the JCVI's 2010 paper are weakened on further reading. The patent application states upfront that the minimal bacterial genome is dependent on a 'rich bacterial culture medium', and in the patent description there is talk of implanting the genome into an enucleated 'ghost cell', which already has a membrane, ribosomes and nucleic acid replication machinery.[6] Similarly, in the 2010 paper, we are told that the synthetic genome will only thrive if it is implanted into an existing cell. It could be concluded that the recipient cell is a crucially important part of the new 'synthetic cell' – that context matters.

Biology as Engineering

The JCVI's work shows the continuities between gene patenting and IP in synthetic biology, but the parts-based approach aspires to develop different ways of owning and sharing biological systems, by attempting to transpose the normative values associated with open innovation regimes into the nascent synthetic biology community.

A definition of the parts-based approach to 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'.[7] The distinction made here between 'parts', 'devices' and 'systems' is the first indication that this approach is heavily influenced by engineering. In fact, one of the most conceptually interesting aspirations of this school is to make biology into an engineering discipline (Brent, 2004).

The guiding aim of this approach is to develop biological components that are standardizsed, interchangeable and can be combined (often called 'BioBricks'), so that new parts do not have to be created in a bespoke manner every time a new biological device is built. In the context of IP, the most important principle adopted by this approach to synthetic biology is modularity. Modularity is not a straightforward concept, but in engineering terms it is defined as a functional unit that maintains its properties irrespective of what it is connected to (Sauro, 2008). A clear demonstration of the modular approach in synthetic biology is the Registry of Standard Biological Parts, a website where information on BioBricks can be downloaded.[8]

There is much discussion in synthetic biology over whether biological systems are actually made of functional modules (Arkin and Fletcher, 2006), or whether they are simply best understood as if they are by the engineering approaches that are adopted in synthetic biology (Morange, 2009). Some argue that modules are favoured by natural selection, as they can

6 In fact, they did not have to use such a ghost cell in their work; instead they manipulated the methylation patterns and restriction systems of the host and donor DNA (Gibson *et al*, 2010).

7 See www.syntheticbiology.org/

8 See http://partsregistry.org/

evolve independently of each other (Hartwell *et al*, 1999; Sauro, 2008), whereas others disagree (Lynch, 2007). There is no consensus on this issue, but whether or not biological systems are actually modular, the question that arises is, can they be made to be so? This is a question that currently guides much work in synthetic biology (Chin, 2006).

As Pottage (2009) has noted, modular systems are well-suited to IP regimes, as 'property lawyers of all species are quite at home with the notion of modularity' (p.169). This is because modular entities are discrete, which makes them easier to describe in patents and to treat as commodities. We see that in applying engineering principles to biology, synthetic biology is making biology better fit with IP regimes (Calvert, 2008). This is not a coincidence because patent law itself developed in the context of industrial manufacturing (Pottage and Sherman, 2007), which synthetic biology models itself upon.

What is particularly interesting about modularity is that it not only lends itself to conventional forms of IP such as patents, but it also 'opens novel ways of imagining the organization of collaborative production' (Pottage, 2009, p. 170). Modular entities are well-suited to commons-based regimes such as open source, because dispersed individuals can work on different modules simultaneously, and they do not have to be highly incentivised to make minor modifications (Benkler, 2002). Thus, we see that commons-based production and private appropriation rely on the very same characteristics.

Ownership and Sharing of BioBricks

As with the JCVI's work on synthetic genomes, computational and informational metaphors are central to the BioBricks strand of synthetic biology. For example, synthetic biologists talk about how DNA can be 'decompiled' through sequencing and then 'recompiled' through synthesis (Specter, 2009), perhaps even 'refactored' (Chan *et al*, 2005). There is also discussion of how 'DNA sequencing and synthesis technologies make genetic information and material interconvertible' (Endy, 2009, p. 7). In addition, it is the ideal of de-contextualised genetic information that synthetic biologists have in mind when they talk about how in the future the transfer of information will be all that will be needed to reproduce biological systems, meaning that transaction costs will become minimal (Carlson, 2010).

The parallels that are drawn to software in the BioBricks field are perhaps not surprising considering that several founders of the BioBricks approach have their origins in the computer industry. Tom Knight, the 'father' of this approach, is a computer scientist who was heavily involved in ARPANET (the Advanced Research Projects Agency Network). Randy Rettberg, who is responsible for the iGEM competition (discussed below) had a previous career at Sun Microsystems (Robbins, 2009). The central role of these key individuals helps explain why software is a common reference point, and why modularity is an important aspiration of the field. The hope is that in the future biological parts will be combined 'in the same manner that Linux modules are now combined to make software' (Maurer, 2009, p. 806). As this reference to Linux suggests, open source is an important aspiration. In fact, when the field was being named in the late 1990s one suggestion was to call it 'open source biology' (Carlson, 2010), partially because early synthetic biology seemed to have some of 'the scruffy hacker ethos that had spurred the personal-computing

revolution' (Ledford, 2010, p. 650). Carlson and Brent (2000) put in an (unsuccessful) application to DARPA for funding for 'open source biology' in 2000, and in this application they talk about the necessity for a 'publicly available kernel' (p.2), again adopting the language of software operating systems. It is notable that while the JCVI's computational metaphors and emphasis on the informational nature of DNA leads them to attempt to gain private ownership of this DNA, similar computational metaphors lead another branch of synthetic biologists to advocate something analogous to open source. I will return to this point below.

Regular comparisons with Linux and open source software are not sufficient to ensure that the BioBricks approach actually does develop along these lines, however. Concerted efforts are needed, and this is where we see work being done to establish the appropriate norms within the synthetic biology community. For example, the BioBricks Foundation has been set up in an attempt to ensure that the information needed to build BioBricks is freely available in the public domain. In addition, the BioBrick Public Agreement (described below) aims to foster 'the *open* design, construction, distribution, understanding, and use of BioBrick™ compatible parts'.[9] Introducing such norms of openness requires novel forms of community building.

Community Building

The most important community-building activity in the BioBricks field is the annual International Genetically Engineered Machine competition, or 'iGEM' for short. This event started in 2003 as an internal competition to MIT, but it has now extended to the point where undergraduate teams from different universities across the globe compete to build the best 'genetically engineered machine', using BioBrick parts. The 2011 competition involved 165 teams with well over 1000 students taking part.[10] What is particularly interesting about the competition is that the aim is to build a community that not only shares a technical approach, but also shares certain values about safety, security and, perhaps most importantly, open access to the technology. Some synthetic biologists are quite explicit about the fact that the competition aims to shape 'the ideology, values and culture of the synthetic biology community' (Smolke, 2009, p. 1099). Teams are rewarded not only for contributing parts to the Registry, but also for 'debugging' existing parts.[11] In this way, a value system is being built into the biological parts (Pottage, 2009). Because BioBricks are designed to be standardised and interchangeable, by creating BioBricks, iGEM teams are providing parts for others to use in the future, and in this way they are embracing the community ethos of open access.

iGEM has grown exponentially since 2003, and it has enthused many young people about synthetic biology and encouraged them to pursue further work in the field (Mitchell *et al*, 2011). In the context of iGEM's success, it is perhaps surprising that it rests on very shaky IP

9 http://biobricks.org/bpa/users/agreement/(emphasis added)

10 See http://igem.org/About

11 One of the requirements for a Gold Medal in the 2010 iGEM was to 'Characterize or improve an existing BioBrick Part or Device and enter this information back on the Registry' (http://2010.igem.org/Judging/Judging_Criteria).

foundations. Many of the DNA sequences in the Registry are already covered by patent claims (Rai, 2009). For example, there is strong IP on Green Fluorescent Protein, an important reporter used by almost all the teams (Chalfie and Prasher, 1996). If iGEM was a for-profit competition then it would undoubtedly be sued for IP infringement. As it is currently an academic venture (with teams requiring an academic institutional affiliation to participate), the incentive for patent holders to pursue litigation is limited, but this threat continually hovers in the background, with the potential to be fatal to the whole operation (Rettberg, 2009). Although some synthetic biologists admit that iGEM is currently breaking the existing IP regime, they do not conclude from this that iGEM should modify itself in line with existing requirements, but argue instead that this demonstrates that the IP regime itself is broken and needs a fundamental overhaul.

The competition is a very important annual event for the BioBricks strand of synthetic biology, and it is unusual that an undergraduate competition (which even sometimes involves teams from high schools), should assume such prominence in a cutting-edge scientific field. However, this is part of the ethos of the BioBricks approach to synthetic biology, because one of its main objectives is to make biology easy to engineer, and to broaden the range of people who can participate in the field. This impulse to broaden participation has resulted a second social phenomenon – the Do It Yourself Biology movement (DIYbio). Discussions of DIYbio, again, often rest on parallels between synthetic biology and open source software (Kelty, 2010). One of the notable features of this sector is that the distinction between developers and users is not sharp (Von Hippel, 2005), thus if synthetic biology is becoming more like software engineering (as its proponents continually stress), this may explain why users are becoming more involved in various different forms of 'biohacking'.

DIYbio is partially enabled by technological developments, which have reduced the cost and increased the ease of access to the technologies needed to do synthetic biology, particularly DNA synthesis. However, more importantly, it represents the aspiration to make biology into a technology that is accessible to all (Bobe, 2010). DIYbio itself is a loose global collective about whom it is difficult to generalise, as it is made up of a mixture of people including 'biocurious' amateurs, artists, 'moonlighting' working scientists, bioentrepreneurs and a few 'hacker culture uber libertarians' (Cowell, 2010).[12]

The increased participation of non-institutional groups in biology can be interpreted as an expression of grassroots enthusiasm and distributed innovation, but it simultaneously gives rise to fears about 'garage biology', misuse and bioterrorism (Ledford, 2010). Making biology easier to engineer makes biology easier for everybody to engineer, and this could include those who have malicious intent. However, arguments are drawn, again, from software to maintain that it is not necessary to restrict access to synthetic biology. A famous quotation in open source software circles is Linus' Law: 'Given enough eyeballs, all bugs are shallow' (Raymond, 2000). Synthetic biologists rephrase this in their own terms: 'our best potential defense against biological threats is to create and maintain open networks of researchers at every level, thereby magnifying the number of eyes and ears keeping track of what is going on in the world' (Carlson, 2010, p. 236).

12 See http://diybio.org/

Motivations for Commons-Based Approaches in Synthetic Biology

The BioBricks strand of synthetic biology embraces openness and commons-based approaches, but when we disentangle the motivations behind this we see that they are diverse. One important motivation is pragmatic. The argument is that a commons-based regime will result in more innovation than a private one (Rai and Boyle, 2007), because the constructions of synthetic biology are likely to require many biological parts, thus if each of these parts was patented this would lead to 'patent thickets' or 'blocking patents' (Oye and Wellhausen, 2009). If biological parts are freely available then this facilitates the development and commercialisation of downstream applications. Parallels can be drawn with the SNP consortium (Henkel and Maurer, 2009), where pharmaceutical companies clubbed together to ensure that very small genetic differences could not be patented (Holden, 2002).

Such pragmatic motivations are often linked to more 'ideological' motivations, to promote 'the cause of radical openness' (Kelty, 2005, p. 199), which stretch beyond the purely economic. According to these motivations, openness is adopted because it is considered the best way to 'benefit all people and the planet'.[13] Ideological motivations also encompass the idea that as biological creatures, we have rights to access to the 'stuff of life'. Endy (2010), for example, talks of 'do it together' biotechnology, and of how accessible technologies empower communities.

The ideological and pragmatic motivations are often rolled together. As with the Internet, both economic growth and greater democracy are hoped to emerge from open biology. Cohn (2005), referring to early discussions of synthetic biology, talks about how there were aspirations that 'the hacker culture values like elegant design, creativity and sharing beneficial works of engineering for all, will spread to biology' (p. 2). Here, we see the desire not only to empower communities in a broad sense, but also to promote certain values such as elegant design and creativity.

A contrasting interpretation of the push for commons-inspired approaches in synthetic biology is that this is merely a way of speeding up the development of a particular school of synthetic biology. This brings to light the important connections between openness and pressures for standardisation. In order to establish common standards, which are needed for the BioBricks approach to progress, it is necessary for these standards to be open (Rai, 2009). If open parts are widely used then there will be investment in complementary parts, as part of a self-perpetuating cycle that will support the development of particular types of part, to the exclusion of others (Maurer, 2009). This 'interoperability' is a requirement of a parts-based approach to synthetic biology, but it also raises the issue of possible anti-competitive behaviour, where one standard comes to dominate (Rai, 2009).

Others argue, however, that the transparency provided by open access will be more likely to *prevent* the field from being monopolised and dominated by large corporations, as GM technology was by Monsanto (Cowell, 2010). This is connected to hopes that openness will lead to broader acceptance of synthetic biology. Carlson and Brent (2000), for example, say that they aim to 'increase the number of citizens who have some sophistication on these issues and can participate in the political choices that increasing biological capacity can

13 http://biobricks.org/

bring' (p.2). The idea of acceptance here is more than just the idea that the 'general public' will provide synthetic biologists with a mandate to pursue their specialised work. The aspirations go much deeper, with DIYbio advocates talking about how in the future parents will be able to re-programme food, and children will design synthetic pets (Dyson, 2007). This line of thought leads to discussion of what it means to be a good 'biocitizen' (Cowell, 2010) in a hoped for era of 'democratization of biotechnology' (Billings and Endy, 2010, p. 1).

Open Innovation

As this discussion illustrates, the idea of 'openness' is a vague one, which is interpreted in many different ways in parts-based approaches to synthetic biology. Following Johnson (2009), it is helpful to make distinctions between three different types of openness. 'Open science' is in the public domain, and outside the IP system. At the moment BioBricks are openly available in this manner from the Registry. 'Open source' depends on a particular IP system (copyright in the case of open source software), and this IP is mobilised, using particular licences such as GNU and Unix, to enable certain legally binding forms of access. 'Open innovation' is much broader, and it refers to a major global change in business models. Open innovation helps to contextualise both open science and open source, and it elucidates important features of BioBricks approaches to synthetic biology.

Open innovation, sometimes called distributed innovation, is often described as being part of the shift we are witnessing from the industrial economy to the knowledge economy, where knowledge has allegedly become more important than land, labour or natural resources (Council of the European Union, 2000; Strathern, 2006). This shift is driven by globalisation and information technologies, and is accompanied by a movement from the centralised organisation of innovation to a recognition of the importance of distributed innovation. This type of innovation is more user-centred, and has the potential to redistribute agency, knowledge and power (Joly *et al*, 2010).[14] Although the paradigmatic example of distributed innovation is open source software, we also see distributed user-centred innovation in areas such as mountain biking, snowboarding (Von Hippel, 2005) and participatory plant breeding (Joly *et al*, 2010). This type of innovation is often discussed by proponents of synthetic biology such as Carlson (2001), because it is seen to resonate with their objectives:

> It is already clear that distributed power generation will soon become more efficient than are centralized systems. Distributed manufacturing based upon local resources will save transportation costs, simplify customization, require less infrastructure investment, and, as a result, will likely cost less than centralized manufacturing. Distributed *biological* manufacturing is the future of the global economy. (p.17, emphasis added)

Open innovation, particularly when tied to open source and open science, gives rise to social goals that are bold and ambitious. There is talk of 'a rapid, radical reboot of the global innovation system for a truly free and open 21st century knowledge economy' (Open Science

14 As Raymond (2000) points out, 'Linux is subversive' (p. 2).

Summit, 2010). Economic arguments are made that old business models are unsustainable, and these arguments often refer to the extraordinary innovation of the internet (Lessig, 2001). Proponents of open innovation maintain that 'the unchecked proliferation of IP rights is perversely out of touch with, and downright inimical to, the collaborative, cumulative, and interdependent essence of innovation in the 21st century's networked knowledge economy' (Jackson, 2010).

Commentators argue that such moves towards openness are likely to have a disruptive effect on current thinking about business models, and that this could change the face of the existing biotechnology industry. Small companies could undermine existing platforms, displacing incumbent multinationals. In this way, open innovation could be socially radical in its consequences, because of the redistribution of power that it could initiate. As Joly *et al* (2010) point out, where there is distributed innovation 'there is a normative model of society being performed as well' (p. 22).

Future Trajectories

This normative model requires a legal framework, and in the last few years the BioBrick Public Agreement has been developed.[15] This is a mechanism for facilitating access to and sharing of BioBricks.[16] In its present version, signing up to it gives contributors access to all the BioBricks in the Registry of Standard Biological Parts, although they must promise not to assert any existing or future property rights that they may hold on BioBricks.[17] What is interesting about this agreement is that it is a contract, and does not follow the norms of open source software licenses, in that it is not 'viral'. This means that contributors to the Registry are not obliged to share on the same terms anything that they take from the Registry and modify, that is, the Agreement 'does not put any encumbrance on downstream uses, such as give-back or share-alike clause' (Smolke, 2009, p. 1102). In this sense, the Registry is more similar to a public domain approach than a copyleft approach (Rai, 2009). Here we see that although synthetic biology is inspired by open source approaches, it diverges from them in important ways.

In addition, according to the agreement, parts can be patented if they are used to produce novel materials and applications.[18] In this way, proprietary systems can be built on an open platform (Smolke, 2009). The explanation given for permitting patenting in certain circumstances is that it will '[e]nable a rich, fully diverse ecology of commercial and public benefit use from the outset' (Endy, 2009, p. 11). This discussion of a 'diverse ecology' helps us understand how the JCVI's proprietary work discussed above fits into the broader synthetic biology landscape. The idea is inspired by the rich ecosystem of software innovation, which is regularly referred to approvingly in synthetic biology meetings. Synthetic

15 http://biobricks.org/bpa/users/agreement/

16 There are other suggestions about how to organize IP around BioBricks aside from the BioBrick Public Agreement (see Rai and Boyle, 2007), such as Henkel and Maurer's (2009) suggestion of embedded Linux, where parts are shared after being kept private for 6 months (again, a direct borrowing from the software world).

17 Those who contributed parts to the Registry could, however, request an attribution from users for future use of their part (http://biobricks.org/bpa/users/agreement/).

18 http://biobricks.org/bpa/faq/#1

biologists like to point out that in software the open source and the proprietary (sometimes referred to in terms of Stallman and Microsoft) happily coexist, and that Google, for example, has both an open source browser and closed search algorithms (Peterson, 2010).

This parallel seems to work, in some circumstances, with the two different approaches to synthetic biology that I have focused on here. For example, one aim of the JCVI's minimal genome work is to develop a chassis into which standardised biological parts can be put, and the genome assembly methods developed by the JCVI have recently proved very useful for parts-based approaches (such as Gibson *et al*, 2009). It should also be noted that there are many different players in the synthetic biology field, beyond the two groups that I have broadly characterised here, and a range of different attitudes towards openness.[19]

A difference between synthetic biology and software, however, is that software is a mature industry, and that Linux and other open source platforms only came into being *after* the technology was established (Bonaccorsi and Rossi, 2003). This raises the question of whether an attempt to impose a 'diverse ecology' on synthetic biology in its early stages will prove successful. Central to the idea of an ecology is that different forms of IP do not only coexist, but also contribute to each other's mutual flourishing. But will this really be the case in synthetic biology? Some synthetic biologists think that we are not moving towards a diverse ecology, but towards a tipping point, where the field will either remain open (not just for the iGEM and DIYbio communities, but also for developing countries), or the IP will be locked up and commercialised for private benefit (Haseloff, 2010).

There are several factors that may encourage us to conclude that synthetic biology is most likely to go down the more familiar path of previous biotechnologies. Powerful multinationals dominate the biotechnology field, and they would suffer from the creative destruction that is predicted to follow in the wake of open biology. Even small synthetic biology companies operate in an environment where they usually require venture capital, and as a result need to file patents to demonstrate that they are a good target for investment (Rai, 2009).[20] As I have shown above, there is a strong tradition of gene patenting in the biotechnology field that can be traced directly to the JCVI's recent patent applications on synthetic genomes.

It would be misleading to portray the patent system as immune to change. Even if patents become the dominant way of protecting synthetic biological inventions, they may start to reflect the extension of gene patenting to cover DNA in its informational form, and they may become more similar to software patents. Eisenberg (2000) argues that such developments would have to be closely scrutinised, as they would represent an illegitimate extension to the immaterial realm of a system originally designed to cover 'bricks and mortar' inventions. They take us far from the view that '[a] gene is a chemical compound, albeit a complex one'.[21]

19 For example, companies such as Arymis Technologies and LS9 are filing patents, and parts registries are being developed by organisations such as the Joint Bioenergy Institute (www.jbei.org/fuels-synthesis/resources.shtml), and the Centre for Synthetic Biology and Innovation at Imperial College (www3.imperial.ac.uk/syntheticbiology).

20 Ginkgo Bioworks, a synthetic biology company, which decided not to pursue venture capital, is a notable exception.

21 Decision of the US Court of Appeals for the Federal Circuit, Amgen v. Chugai Pharmaceutical Co., 927 F.2d 1200.

Although there are strong precedents that might encourage us to conclude that the patent path is the one that synthetic biology is most likely to take, we should not overlook the forces pulling in the other direction, towards open and distributed innovation. Synthetic biology may be the pressure point where dissatisfaction with the current system of IP protection in biotechnology comes to a head. As we saw above, one of the conclusions drawn from the iGEM competition is that the current system is broken and requires a fundamental overhaul. The increasingly broad range of actors participating in the life sciences – from engineers to computer scientists to undergraduates to citizen scientists and artists – may well have consequences for IP regimes.

Conclusions

The speculative nature of this discussion is indicative of the uncertainty involved in studying a field that is currently in the process of inventing itself and its ownership regimes. One of the most profound uncertainties at the heart of this discussion is the scientific and technical feasibility of the project of synthetic biology itself. The social and normative innovations being developed around BioBricks approaches to synthetic biology rely on the ability to make biological entities into standardised modular parts. However, the field is continually being challenged by those who think that biology is simply too complicated to be standardised in this manner. A recent article called 'Five hard truths for synthetic biology' (Kwok, 2010) points to the unpredictability and unwieldy complexity of noisy biological systems, where context-dependence is crucial and where it is very hard to insulate parts of the system from each other to such an extent that interactions may actually be more important than parts in biological systems.[22] We saw above how similar issues arose in the work of the JCVI, because cellular context and a 'rich bacterial cultural medium' are essential for synthetic genomes to work, weakening the assumption that DNA can be thought of as the 'instructions for life'. Literature from philosophy and the social sciences also challenges the appropriateness of the application of informational and computational metaphors to living systems, and criticises this 'flattened' understanding of the biological.

This article has argued, however, that the very same metaphors can be put to vastly different political and social purposes by different groups, and that they can underlie contrasting, sometimes even opposed, property regimes. We saw how informatic metaphors were recently drawn upon to argue against Myriad Genetics' patents on breast cancer susceptibility genes. In synthetic biology, proponents of open source inspired distributed innovation draw on these metaphors to assert the importance of the free availability of genetic information. However, the same informational metaphors also expand the repertoire of 'property talk' for groups such as the JCVI that wish to extend IP protection in synthetic biology beyond the traditional grounds of 'composition of matter'.

This means that it is not sufficient for scholars of science and technology to simply critique the use of informational metaphors in synthetic biology. Instead, it is necessary to be alive to their indeterminacy and examine the work that they are doing in different contexts. We should also not underestimate the performativity of these metaphors, or the potential for

22 Synthetic biologists are keenly aware of these difficulties and are in fact heavily quoted in the Kwok article.

synthetic biologists to turn 'tropes into worlds' (Haraway, 1994, p. 60). Whether or not these metaphors are appropriate ways of understanding existing biological systems, synthetic biologists are attempting to realise them in their biological creations. In other words, biology is becoming more like software because it is being engineered to be more like software.[23] Whether synthetic biology will succeed in its objectives is an empirical question. If it does succeed, it may be necessary to rethink our current notions of the 'biological'.

I have shown that there are several different routes that ownership and sharing in synthetic biology could take, and which is followed will depend on the success of both technical and social innovations. It will be extremely interesting to see whether this field will follow the precedent set by gene patenting, whether a diverse ecology of the open and the proprietary will flourish or whether the confluence of engineering, biology, software and community-building will lead to a participatory and distributed approach to innovation in synthetic biology.

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23 Similar points are also made by Walby (2001, p. 790) and Torrance (2010, p. 647).

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