Chapter 5

Intellectual property issues and synthetic biology

Business models for synthetic biology need to address intellectual property. There is an apparent tension between the desire for "openness" and freedom of access to new parts and the need for intellectual property (IP) protection to allow companies to protect their investments and form the basis for developing their business. Patenting has for decades been a difficult area for life science business. Some envisage that synthetic biology will require a broader range of instruments: trademarks and industrial designs, copyrights, materials transfer agreements and database protection. However, a clear message from the IP community is that, although synthetic biology may present its own challenges, the global IP system is likely to be able to cope and is not under any serious threat. There are identifiable roles for government policies, especially in improvements to access and technology transfer.

> "Today the United States Supreme Court ruled on the validity of BRAC1 and BRAC2 human gene patents stating that, 'A naturally occurring DNA segment is a product of nature and not patent eligible merely because it has been isolated, but cDNA is patent eligible because it is not naturally occurring,' is consistent with our views on gene patents and is one we support. This ruling is good news for the biotech industry as it clarifies the rules and reduces uncertainty."
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> J. Craig Venter, Ph.D., Founder and CEO, Synthetic Genomics Inc. and Founder and CEO, the J. Craig Venter Institute
> www.syntheticgenomics.com/media/press/061313.html, 13 June 2013

Introduction

Business models in synthetic biology will have to address the question of intellectual property (IP), especially, but not exclusively, patenting. Biotechnology patents emerged from the pharmaceutical field, an unusual technological field that draws heavily on university science, venture capital financing, the production and marketing capabilities of global pharmaceutical firms, and skills in translational science developed by smaller, more nimble, science-based start-ups (Ebers and Powell, 2007). The field is characterised by rapid growth, complexity and comparative youth, and the participants tend to attach a high degree of importance to IP (Arora et al., 2008). Also, venture financing in biotechnology appears to be linked to patents (Kumar and Rai, 2007). The industry collectively submits a large number of difficult, highly technical patent applications, which makes it hard for patent examiners to pare down broad claims and weed out applications that do not meet statutory patentability criteria (OECD, 2005). Moreover, patents making very broad, prophetic claims have the potential to stifle innovation.

Companies can and do use trade secrets and first-mover advantages, or lead time, as alternative strategies to formal patenting. Even though a patent is supposed to protect against imitation, in practice it does so imperfectly, and secrecy may be a preferred strategy. In a survey conducted by Arundel (2001), although secrecy was the leading strategy, a substantial number of companies rated patents more highly than secrecy and many rated patents and secrecy as equally important. The semiconductor industry is a suitable comparative test case for synthetic biology as it is characterised by technological sophistication and extremely short product life cycles. Hall and Ziedonis (2001) noted that US companies in the semiconductor industry tend to rely more on measures such as lead time, secrecy and design capability than on patents. In terms of patenting, synthetic biology may resemble the semiconductor industry and other complex engineering industries more than biotechnology.

Because patents are used to derive measures of innovative capability, there is a danger that it is the propensity of a firm to patent rather than its ability to innovate that is measured (Zheng et al., 2010). However, a strong IP background is an important draw for venture capital investors. There is also some evidence to show that innovative capability is highly correlated with the growth potential and long-term performance of high-technology start-ups. In a Canadian study, Baum and Silverman (2004) showed that biotechnology start-ups with more patents, both recent and older, obtained significantly more VC financing. VC therefore appears more likely to be invested in start-ups with a strong history of patenting. Patents are also important for attracting finance for universities and research institutions specialised in research.

The question of patentability in synthetic biology

The patentability of genetic materials was examined by the United States Supreme Court and the Board of Appeal of the European Patent Office (EPO) between the 1970s and the 1980s. The issue ignited a heated political debate, with the involvement of citizen groups. The core issue is whether substances that exist in nature, such as DNA and genes, should be patentable.

Substances existing in nature are patentable in the United States, Europe and other OECD countries. However, the patentability of "substances existing in nature" falls under the Trade-Related Aspects of Intellectual Property Rights (TRIPS) flexibilities and is subject to different interpretations. It means that World Trade Organization (WTO) member countries are not obliged to grant a patent to substances from nature, even if they are isolated and purified (Correa, 2000).

Table 5.1. Patentability of substances existing in nature

Non-patentable "substances existing in nature" are excluded from patentability	Specific provision on the patentability of subject matter consisting of or deriving from naturally occurring products	
	excluding	allowing
Argentina, Brazil, Chile, Djibouti, Dominican Republic, Egypt, Guatemala, Honduras, India, Israel, Laos People Democratic Republic, Mexico, Nicaragua, Oman, Pakistan, Panama, Portugal, Thailand, Tunisia, Uruguay, Zambia, Zimbabwe, Andean Community, OAPI (African Intellectual Property Organisation)	Argentina, Brazil, Chile, Costa Rica, Egypt, Pakistan, Panama, Rwanda, Uruguay, Andean Community	Albania, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, San Marino, Serbia, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, The Former Yugoslav Republic of Macedonia, United Kingdom, European Union

Source: Adapted from WIPO (2011), "Patent-related flexibilities in the multilateral legal framework and their legislative implementation at the national and regional levels" , Part II, CDIP/7/3, Geneva.

Concerning the TRIPS flexibilities on the patentability of substances existing in nature, the Committee on Development and Intellectual Property (CDIP) of the World Intellectual Property Organization (WIPO) conducted a survey and provided a sample of TRIPS flexibilities in use (WIPO, 2011). The survey targeted 185 WIPO member countries and regional patent offices, and asked whether substances existing in nature are explicitly excluded as patentable inventions (Table 5.1), and whether there are specific provisions on the patentability of subject matter consisting of, or deriving from, naturally occurring products (allowing or excluding).

Synthetic DNA sequences are therefore more easily patentable than DNA sequences derived from natural sources. One of the main criticisms of the patent system in biotechnology was whether patents should be granted to products of nature, because products of nature are "discoveries", which are not patentable. In synthetic biology, however, DNA sequences, systems, cells and organisms are designed by humans. Human-made DNA sequences can therefore receive patent protection without touching on the issue of discovery from nature. According to Torrance (2010), "Genes constructed using synthetic biological techniques will have their origins in human imagination and will, thus, not be products of nature… synthetic genes would remain patentable subject due to their non-natural origins." While the ethical justification of DNA synthesis may be debatable, synthetic biology does not fall under the scope of general exclusion from patentability, such as "inventions contrary to public order or morality".

Complexity of the synthetic biology patent landscape

The J. Craig Venter Institute patent on the minimal genome bacterium (US Patent Application 20070122826),[1] i.e. the smallest genome needed for a living organism, is an example of a fundamental patent. The fundamental patent covers the basic starting point of technology and could frustrate follow-on research. Such fundamental patents can have detrimental effects on associated research. An early warning system at patent offices that would check for the emergence of such broad patents would be a useful tool (see Box 5.2).

Patents have already been granted on many of the products and processes involved in synthetic biology. For example, a report of the ETC group (2007) shows examples of patented inventions in synthetic biology: patents on methods of building synthetic DNA strands;[2] patents on synthetic cell machinery such as modified ribosomes;[3] patents for the engineering of biosynthetic pathways;[4] patents on new and existing proteins and amino acids;[5] patents on nucleotides that augment and replace the letters of DNA.[6]

Software infrastructure in the synthetic biology laboratory deserves special attention from the patent perspective. Currently, synthetic biologists use multifaceted software: there is software for circuit design and implementation, circuit optimisation, DNA and RNA design, protein design, and integrated workflows. Software patents are a problem not only because their number is increasing,[7] but also because patent laws in jurisdictions around the world are not clear on the scope of patent protection on software.

Discussions among lawyers to define the boundary between software that is or is not patentable have reached no clear conclusion. The starting point of deciding on the patentability of computer-related inventions is the rule that abstract mathematical methods and algorithms are outside the scope of patentable subject matter. However, pressure to patent software-related inventions emerged, especially when a patent was granted for business method inventions based on software in the United States.[8]

Software patents are often cumulative and prevent other people from using the patented technologies. However, as innovation in synthetic biology is inclined to be open, the software infrastructure needs to be accessible to researchers. Software patents in synthetic biology need to be analysed in terms of enhancing transfer of knowledge.

Open innovation and open source

The open innovation paradigm is built on the assumption that individual companies do not have the financial resources and personnel to carry out certain complex innovation projects on their own and must share knowledge, ideas and inventions with other companies (Chesbrough, 2006). Open innovation is usually contrasted with closed innovation, supposedly its predecessor, where companies generate their own innovation ideas and then develop, build, market, distribute, service, finance and support them on their own (Chesbrough, 2003). While truly closed innovation was never the rule, trends such as outsourcing, agility and flexibility have forced companies to become network organisations. With the rise of globalisation and the development of improved market institutions for trading ideas, and the appearance of new technologies for collaborating across geographical distances (Dahlander and Gann, 2010), the do-it-yourself mentality in innovation management became obsolete. Even a company of the size and resource intensity of IBM sometimes relies on open innovation and open source.

In synthetic biology, the massive infrastructure and business tasks involved in getting a product to market calls for an open innovation model ranging from engineering at the nano level to building refineries and large-scale plant to getting customers to buy the products. As a result, investors often respond positively to alliances with other firms who possess comple-

mentary resources such as financial, research and marketing capabilities (Chang, 2004). This complementarity is likely to be a defining feature of synthetic biology open innovation.

A high degree of complementarity (e.g. a synthetic biology biocatalyst producer and a large-scale chemical process technology company) and a blend of small and large organisations (e.g. for the small company to gain access to a large customer base and new geographical markets) seem critical to the new synthetic biology companies. Moreover, biotechnology is notorious for long lead times to market, and open innovation could reduce development times by allowing small companies access to the resources of large ones. For example, GlaxoSmithKline's Open Lab Initiative is designed to host 60 visiting scientists from academia or the biotechnology industry and provides access to the corporate compound collection (So et al., 2011).

However, a fundamental contradiction in openness has significant implications for synthetic biology. Kumar and Rai (2007) called it the Synthetic Biology IP Puzzle. On the one hand, intellectual property law insists that certain types of material remain in the public domain. On the other, individuals attempt to use intellectual property rights (IPRs) to create a commons, just as developers of free and open-source software use the leverage of software copyright to impose openness requirements on future programmers. Intellectual property policy specifies items, such as abstract ideas or compilations of unoriginal facts, that cannot be covered by IPRs precisely in order to leave them open to all. Yet many open source techniques require property rights so that future users and third parties will be bound by the terms of the licence. Kumar and Rai ask if this indicates a need to rethink the boundary between intellectual property and the public domain.

As it concerns software development, open source means that people have access to the source (fundamental) software code and can use it to modify, sell or give away new products without paying license fees. These new products, however, must also make their source code available and extend the same licence agreement to others. In effect, open source is covered by a specific, open form of IP, which is often called a public licence. For example, Netscape released its browser source code under the Netscape Public License, which in turn was developed into Firefox. Other examples of important products developed using the open source innovation method are Linux, Apache HTTP Server and Internet Protocol. Far from being unregulated, the system relies on existing IP and legal contracts, as copyright exists in the source code and the contract to ensure that a free licence is itself a legal tool.

The peculiarities of the parts agenda

Nowhere else in the life sciences is the ambition to standardise parts as pronounced as in synthetic biology. There is a frequent, almost universal, comparison to the electronics industry. However, while the technological benefits of introducing electronics methods to biology are clear, the economic benefits of standardising parts are less so. The cost of parts is at the heart of the matter, as well as the rate at which their cost drops the more they are used. A danger for the industry is the creation of a parts monopolist, which has been a feature of the electronics industry. Synthetic biology companies would have no desire to share their earnings with a parts monopolist. Henkel and Maurer (2007) argue that this is good reason for synthetic biology companies to donate resources to a Linux-style "open parts" collaboration. But they also note that there would be circumstances in which the simple Linux model based on own-use incentives would not work.

Because there are different levels in the hierarchy of biological structures, from individual molecules to whole cells, tissues and organisms, the patented information and tangible materials may cover different levels of the hierarchy, from DNA to parts, devices and systems. As a consequence, synthetic biology products could involve hundreds of different parts protected by different patents or copyright held by different rights holders. The situation is similar to a technical area such as semiconductors, and raises issues such as patent thickets. To the extent that they cover standards that synthetic biologists wish to establish, both foundational patents and patent thickets are likely to be problematic. Companies using their IP can also acquire related IP in order to create a patent thicket and a barrier to entry to potential rivals. Even assuming appropriate enforcement of foundational patents, a proliferation of patents on basic parts and devices puts high transaction costs on such thickets. Also, patents can compound the tendency of network markets to tip into monopoly, technically inferior products or other pitfalls (Henkel and Maurer, 2007).

Of interest to the MIT Parts Registry is non-assertion statements by other patentees. Recent non-assertion statements have been made by IBM, Sun Microsystems and other companies to indicate that they will not assert their patents against anyone working on open source software. In the IBM Statement of Non-Assertion of Named Patents Against OSS, IBM pledged the free use of 500 of their US patents, as well as all counterparts of these patents issued in other countries for the development, distribution and use of open source software, owing to their belief that the open source community has been at the forefront of innovation (www.ibm.com/ibm/licensing/patents/pledgedpatents.pdf).

Another potentially problematic issue is the 20-year protection period. However, a much more limited, metered protection already exists. Indeed, the available maximum patent life is not relevant for the majority of patents because the value of the intellectual property falls to zero, either because of technical redundancy or commercial non-viability (Greenhalgh and Rogers, 2010). The Linux General Public Licence does not require software companies to disclose their code to the general public until the devices containing it have reached the mass market. This creates an 18-month window in which the code remains proprietary. With a similar model for synthetic biology, the part maker would get protection long enough to get the reward before the protection disappeared. This seems to work as a reward model in Linux, and adaptations may work in synthetic biology (e.g. adjustment of the metered protection period).

Patent pools

The essential premise of the patent pool is that a series of patents relating to the use of a particular technology are collected so that they can be efficiently licensed to those making, using or selling the technology. The distinctive feature of the patent pool is the bundling of IP rights.

Patenting in various industries led to the idea that patenting can ultimately discourage innovation. The patent pool phenomenon arose from the need to overcome strategic behaviour by patent holders that blocked the development and sale of a new product. Patent pooling evolved with time, and a form of patent pool arose when companies wished to create common technological standards for an industry. This form of patent pool became common in the electronics industry, which now has clear technological standards. The relevance to synthetic biology, with the often-repeated need to create standardised parts, is obvious.

In the pharmaceutical industry, by contrast, it is argued that patents are particularly effective because there is typically a one-to-one mapping between chemical structure and the action of a given drug that makes inventing around difficult (Levin et al., 1987). Synthetic biology may fall between these categories. While there has been broad interest in patent pools in the life sciences, it has been difficult to create and maintain them. The life sciences and their translation into biotechnology products still require as broad a flow of basic scientific information as possible. But the need for standardisation in synthetic biology shows that patent pooling and other forms of knowledge networks and markets have a significant role to play and may shape the business models of synthetic biology companies.

The difficulties for life sciences patent pools appear to be particularly acute in human health biotechnology. The best-known life sciences patent pools have had a clear philanthropic purpose. In these early days of the development of synthetic biology companies, a clear lead seems to have been gained by those operating in industrial biotechnology, in particular those that are creating novel biofuels products or processes. This again may favour a particular type of behaviour. It has been previously opined (OECD, 2002) that patent pools may only be effective in the life sciences if there is a limited field of application and essential patents can be defined. In applying synthetic biology to biofuel products and processes, or more widely to bio-based products, those conditions may be met, but there are also situations where they may not. Therefore alternative mechanisms are essential for synthetic biology.

Open licensing, standardised licensing and licensing principles

Licensing guidelines can be published to streamline licensing activities in the life sciences, and licensing practice remains the most effective means of providing access to IP-protected technologies.

BioBrick Public Agreement (BPA)

The BioBrick Public Agreement[9] is a free standardised legal contract that allows individuals, companies and institutions to make their standardised biological parts free for others to use. According to the Foundation, "the BioBrick Public Agreement was developed for sharing the uses of standardised genetically encoded functions (e.g. BioBrick parts) but, in practice, can be used to make free the sharing of any genetically encoded function that you might already own or make anew". The agreement clearly states that the mission is to promote the development of synthetic biology as a field under the principle of openness in ways that benefit the world.

The BioBrick Public Agreement attempts to minimise legal uncertainty and to avoid disputes arising over ownership, IPRs and attributions, such as open source and free software licensing. According to Torrance (2010), this agreement could be seen as an "initial effort to draft a legal constitution to guide the beneficial development of the field of synthetic biology".

Creative Commons

RIKEN uses the Creative Commons licensing scheme for its gene design competition GenoCON. RIKEN licenses the newly designed DNA information through Creative Commons licensing "CC BY-SA (Attribution-Share Alike)". Licensees can use or alter the information, even for commercial purposes, as long as they identify the licensor and license their new inventions under identical terms.

BiOS

Biological Innovation for Open Society (BiOS)[10] promotes open source, open science, and open society. A BiOS licence is a legal framework to share patented and non-patented technology, including materials and methods. BiOS created a patent-based commons, called protected commons. The members of BiOS agree to responsible sharing and agree not to assert IP rights against other members of the commons for the use of technology for their research and further improvements.

Freemium

Toyoda (2011) extended the application of the so-called "freemium platform" to synthetic biology. A freemium platform takes different forms, with varying tiers from free to premium services, hence the term freemium. A free version of the service needs to be provided to contributors such as scientific and educational communities, while a premium or expensive version of the service will be required of those who receive the benefits from open innovation on the platform. For digital products, the ratio of free-to-paid services is very large in terms of the number of users. A typical online suite follows the rule that a small percentage of users support all the rest. In the freemium model, this means that the beneficiary pays for the premium version to support the platform, while many external contributors receive free access to the online services. The reason this works is that the cost of providing the online services is close enough to zero to be considered negligible. Thus, in a suitable freemium model, only a premium user can organise an open innovation project on the information platform, while free users cannot do so, but can participate as contributors to the project.

Influence on the licensing conditions by the funding agencies and the philanthropic organisations

Governments and philanthropic organisations (e.g. the Bill and Melinda Gates Foundation, see Annex A) financially support research and commercialisation of synthetic biology. IPRs are handled by the legal team of the Gates Foundation and are negotiated as part of the contractual agreement. The basic principle is that all scientific and technological advances should be distributed and disseminated as widely as possible. The intellectual property arrangements should contribute to this goal.

The Gates Foundation makes no claim on the IPR and is not opposed to companies profiting from the results as long as the desired impact is achieved. Pharmaceutical companies, for instance, can profit from selling the drugs they have agreed to sell at marginal prices in developing countries by selling them at market price in developed countries. In other words, IPR

policy is flexible but based on certain principles related to global access. The Foundation discusses this with the technology transfer office or lawyer, which then negotiates with the company or the university.

Patent clearing houses

In a field such as synthetic biology, in which one engineered microorganism might involve hundreds of different parts and processes and therefore various IPRs and stakeholders, freedom to operate (FTO) may be unclear and therefore hinder innovation. Specific problems include high transaction costs (identification, negotiation, enforcement), legal uncertainty, high royalties and royalties stacking (van Zimmeren et al., 2011). Determining what is already covered by patent rights is a particularly acute problem, but there is some hope that modern text mining and computer-search technologies will help to make analysis of FTO easier and economically more feasible (Rutz, 2009).

The notion of an FTO survey, which arose in the United States, is a sort of patent clearance search to confirm compliance with IP law. A clearance survey on the possibility of infringing a third party's patent is traditionally conducted when planning to put commercial projects on the market, but it is frequently conducted much earlier, even at the R&D stage.

In June 2010, the symposium of the National Academy of Sciences and the National Academy of Engineering, "Synthetic Biology for the Next Generation", made recommendations on IP management for the synthetic biology community. One of their recommendations was the creation of clearing houses. The idea is that a patent clearing house, organised by a third party, accepts the registration of synthetic biology inventions, both sequence and functional claims. Typically the functions of the clearing house would be to match licensees with licensors, offer standardised licences, collect and distribute royalties, enforce patents, and offer dispute resolution via mediation and arbitration. The incentives for users are safe harbours. Users of synthetic biology inventions though the clearing house would be exempted from patent infringement. The incentive for patent owners is assurance of their right to claim royalty fees and lower transaction costs. The recommendation came from a stakeholder group comprising government, industry and scholars that had met in Stanford in the previous year. Box 5.1 shows some other recommendations from the symposium.

Box 5.1. Synthetic biology for the next generation

At the "Synthetic Biology for the Next Generation" symposium (12-13 June 2012), legal scholars Farahany and Lemley proposed IP schemes for synthetic biology:

1. Creation of third-party patent clearing houses.
2. Refining statutory governing schemes: make exemption from patent infringement liabilities for: i) mere information providers who offer or sell synthetic biology inventions; and ii) third parties that assemble tangible materials based on the instruction provided by others, and iii) statutory research and educational use exceptions.
3. Introduction of petty patents (utility models) in synthetic biology: Under the current patent system, the high costs of obtaining IP protection and long prosecution processes may have a detrimental effect on synthetic biology and the biotechnology industry. Utility models may work well for synthetic biology, because they can be registered quickly without examination and may save costs, without royalties stacking.

Source: NAS (2012), "Synthetic Biology for the Next Generation" symposium held on 12-13 June 2012, transcript from online video: http://events.tvworldwide.com/Events/IOM/NAS120612.aspx.

Government policies to improve access

Open access, open publishing policy

US National Institutes of Health PubMed Central

In April 2008, the National Institutes of Health (NIH) implemented a policy requiring all NIH-funded researchers to make available to the public an electronic version of their final, peer-reviewed manuscripts accepted for publication by depositing the manuscripts in the National Library of Medicine's PubMed Central within 12 months of the journal's publication. Recent research on the NIH's policy confirms that "openness" has positive impacts on follow-on research, innovation and commercialisation (Committee for Economic Development, 2012).

Similar policies to increase public access have been implemented in other OECD countries: European Research Council (European Union); Medical Research Council (United Kingdom); Biotechnology and Biological Science Research Council (United Kingdom); Wellcome Trust (United Kingdom); Hungarian Scientific Research Fund (Hungary); Austrian Science Fund (Austria).

Improving technology transfer

The Lambert Toolkit

National patent offices may facilitate technology transfer by providing standardised licensing models. For example, the United Kingdom Intellectual Property Office was involved in creating the Lambert Toolkit to enhance business–university collaboration (www.ipo.gov.uk/lambert). The toolkit is a set of model agreements and governance structures prepared by the Lambert Working Group on Intellectual Property to highlight opportunities for business–university collaboration, identify successful business–university collaborations that could serve as role models, and offer ideas to stimulate debate and shape policy. The United Kingdom Intellectual Property Office hosts the Lambert Toolkit on its website. This collaboration takes advantage of national regulatory infrastructures and is a model that policy makers can refer to when designing technology transfer systems.

The objectives of the toolkit are to facilitate negotiations between potential collaborators, reduce the time and effort required to secure agreements, and provide examples of best practice. The toolkit consists of a set of five model research collaboration agreements (one-to-one collaborations) and four consortium agreements (multi-party projects). The five research collaboration agreements provide different approaches in terms of ownership or the right to exploit the intellectual property and the contributions (financial or other research assets) that result from the collaborative project. The model agreements also address issues such as liability, state aid, tax credits, confidentiality and publication.

Competition policy: A new form of mandatory license

When universities and companies manage their IP on an exclusive basis and do not contribute to the dissemination of technology, other centres, genetic testing laboratories, and low-margin national laboratories may be excluded from the market (Carbone et al., 2010). Compulsory licensing, which gives non-voluntary authorisation to use patents to accelerate the diffusion of technologies, is rarely used by OECD governments. Recently, however, France and Belgium drew up national laws giving government statutory authority to force patent owners to license patents, if failure to do so would threaten public health (Carbone et al., 2010).

Other forms of IPR relevant to synthetic biology

For synthetic biology, IPR issues extend well beyond patenting and increasingly include copyright, design rights, trademarks and data exclusivity.

Copyright

Copyright may be applicable to two of the main technologies of synthetic biology. First, software receives copyright protection in addition to patent protection, although the basic rule is that an "idea" is not copyrightable, but that the "expression" of an idea should be within the scope of copyright protection. Despite this basic rule, software is considered to meet the "expression" requirement and to be protected under copyright law.

Second, copyright may be applied to DNA sequences, although the products of synthetic biology are not yet discussed as copyrightable subject matter in the courts (Kumar and Rai, 2007). Torrance (2010) reports that DNA, genes, arrays of genes and genomes fit into the "literary works" category, both generally and as computer programmes, in several significant ways. A synthetic biologist might consider DNA sequences to be a form of computer software. Given that one of the primary goals of synthetic biology is to engineer cells and genes to become ever more like computer software, DNA sequences will likely move towards copyright by analogy to computer software. An implication for synthetic biology research is that the exceptions to copyright, such as fair use or research use exceptions, need to have clear boundaries and offer safe harbours for free research.

Protection of databases

Databases receive legal protection that varies from country to country. Databases may be protected under copyright law, laws on prevention of unfair competition, or *sui generis* data protection laws. When companies invest time, costs and effort in gathering and storing data, the results of such efforts deserve legal protection. However, data need to be shared in the research community.

For example, the information biology group of RIKEN (Japan) maintains databases for genomes and proteins (Scientists' Networking System, SciNES), and opens them for research purposes, including research competitions organised by RIKEN. RIKEN aims to provide a basic database for rational genome design based on the RIKEN SciNES and offers programmes for designing the sequence of genomes as "open source programmes".[11]

Trademarks and industrial designs

Trademarks can play a role in synthetic biology by distinguishing the scientific, technological and research services offered by certain institutions. For example, BioBricks® is a registered trademark. When scientists, students or the general public seek biological parts under the "Biobrick" word and logo, they expect the parts to come from the BioBricks Foundation, and consider that the Foundation controls their quality. In this way, trademarks associated with certain services in synthetic biology have value.

Johnson (2009) pointed out that industrial design rights may be relevant to synthetic biology when interoperability is required. In Europe, however, industrial design protection is not applied to "must-fit" parts that need to fit to work together, e.g. plugs and sockets, or to "must-match" parts, where the appearance of an article is an integral part of the other object, e.g. a door and a car body.

Protection of confidential information and material transfer agreements

Undisclosed information, also known as trade secrets, is an integral part of intellectual property protection in the life sciences. Undisclosed information on research, data and methods can be protected by *sui generis* trade secret law, which prevents the unauthorised transfer of undisclosed information. Undisclosed information is often a critical part of technology transfer between scientists and companies.

In addition, materials that are covered or not covered by patents are often transferred through material transfer agreements (MTAs). In such cases, undisclosed information can be protected through contractual provisions, such as confidentiality agreements. However, gathering and analysing the information required to guarantee freedom to operate for an MTA has become prohibitively expensive for a single part, and would economically unviable for complete devices. This is becoming a burden for commercialisation. What is needed is a minimal and universal MTA so that the flow of parts is easy and cheap.

At a workshop on "Synthetic Biology, Innovation, and Intellectual Property: Towards a UK Strategy Workshop Report", IP issues associated with synthetic biology were discussed and a small number of targeted recommendations were made (Box 5.2).

Box 5.2. "Synthetic Biology, Innovation, and Intellectual Property: Towards a UK Strategy" Workshop, London, June 2013

At this workshop it was generally agreed that there was nothing about synthetic biology that would necessitate an overhaul of the IP system. Three specific recommendations can be carried forward by the UK Synthetic Biology Leadership Council to the Technology Strategy Board and the Department for Business, Innovation and Skills.

1. *Synthetic biology IP watching function*

   The United Kingdom could benefit from a synthetic biology IP watching function that is similar to IP Watch (www.ip-watch.org/) or sector-supported consortia but focused on synthetic biology issues in the United Kingdom. The synthetic biology IP watch would perform several functions. First, it would provide timely reports on synthetic biology patent applications and patents granted in the relevant jurisdictions (UKIPO, EPO, USPTO, JPO). Second, applications with the potential to become blocking patents could be identified and comments submitted to patent offices. Third, the IP watch would periodically present consolidated reports on what is considered non-obvious in synthetic biology IP and how multidisciplinary teams in IP offices are being organised to examine applications. Fourth, it could identify and track emerging issues in synthetic biology IP, including changes in patent prosecution and patent challenges. It could develop education and outreach mechanisms to benefit researchers, institutions of higher education, funding councils and firms through the collection and dissemination of information relevant to innovation in synthetic biology. It could be established on the initiative of the Technology Strategy Board, with the expectation that it would ultimately be supported through a public-private partnership.

2. *Identification of synthetic biology value chains*

   Work on the identification of value chains for synthetic biology needs to be undertaken immediately. In fields such as pharmaceuticals and fine chemicals there are established value chain models in which the role of IP is reasonably well understood, even if that role is viewed as problematic or in need of optimisation. Inventions and discoveries in synthetic biology will introduce new opportunities for commercialisation, yet it is unclear if value chain archetypes for other technologies will apply. Adoption of information and communication technology archetypes in the context of biotechnology innovation has proven unsuccessful, and it is now apparent that the R&D and firm strategies for innovation in the life sciences are different. The development of examples of value creation in synthetic biology, ideally concentrating on UK firms, would generate synthetic biology archetypes. These would be useful in exploring links between IP and synthetic biology innovation, and would provide a context for interpreting open access and innovation policies arising in UK and Horizon 2020 synthetic biology initiatives.

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Box 5.2. "Synthetic Biology, Innovation, and Intellectual Property: Towards a UK Strategy" Workshop, London, June 2013 *(continued)*

3. *Evaluating potential strategies for blended IPRs*

   A consequence of the recognition of biology as an information science is the temptation to think of ways to apply copyright to biological information. Although this was previously not feasible as an alternative to patenting genes, creating and transcribing synthetic sequences raises questions about copyright of "biological expressions". As synthetic biology develops, the integration of biological with automated machine systems increases the importance of software IP. Envisioned, then, is a future in which commercialisation of synthetic biology involves the stacking of different kinds of IP rights in single products in ways that do not have obvious correlations in contemporary technology. Although this may not occur until sometime in the future, it is serious enough to warrant consideration, perhaps in a scenarios format, of the implications for open access and innovation policies, behaviour of institutions of higher education, venture capital and firm strategies.

Source: Workshop summary document, Innogen, Edinburgh.

Conclusion

This chapter may give the impression that IP issues in synthetic biology are very difficult. This is not the case. There are specific problems or potential problems, but there are also solutions or potential solutions. There is no need to reform the IP regime. The synthetic biology community and IP professionals can learn from the semiconductor and other industries that have solved similar problems. But the issues will have to be tackled in a systematic and timely manner to prevent the formation of commercial barriers at a time when many stakeholders are watching synthetic biology closely. The toughest issue will be achieving international agreement on allowing the free flow of information to maximise progress.

Notes

1. US 20070122826: Minimal bacterial genome. Assigned to J. Craig Venter Institute, Inc.
2. For example, US 6, 521, 427: Method for the complete chemical synthesis and assembly of genes and genomes. Assigned to Egea Biosciences, a subsidiary of Johnson and Johnson.
3. For example, WIPO Patent WO05123766A2: Methods of making nanotechnological and macromolecular biomimetic structures. Awarded to Alexander Sunguroff.
4. For example, WIPO Patent WO05033287A3: Methods for identifying a biosynthetic pathway gene product. Claimed by The Regents of the University of California, or US 20060079476A1, US patent application entitled, "Method for enhancing production of isoprenoid comoonds."
5. For example, WIPO Patent WO 06091231A2: Bio-synthetic polypeptides utilising non-naturally encoded amino acids (2006). Awarded to Ambrix, Inc.
6. For example, US 5, 126, 439, "Artificial DNA base pair analogues," awarded to Harry P. Rappaport; and S. Benner, U. Patent 6, 617, 106, "Methods for preparing oligonucleotides containing non-standard nucleotides."
7. The number of registered computer-related patents (G06F17/60 and G06Q) was around 288 in 2000, but increased to 2 562 in 2009. Bessen and Hunt (2004) say that the number of software patents issued in the United States was 765 in 1976 and increased to 24 891 in 2002.
8. State St. Bank and Trust Co. v. Signature Fin. Group, 149 F. 3d 1368 (Fed. Cir. 1998).
9. https://biobricks.org/bpa/.
10. www.patentlens.net/daisy/bios/home.html.
11. RIKEN's SciNES is a cloud web system built on the next-generation web standard "semantic web" which offers the research community a networking system. SciNES contains many virtual laboratories and researchers can create their own database without creating and maintaining a web server themselves. The SciNES virtual laboratories aim to enhance international research collaboration among researchers. RIKEN's GenoCon offers SciNES to participants in the competition (www.riken.go.jp).

References

Arora, A., M. Ceccagnoli and W.M. Cohen (2008), "R&D and the patent premium", *International Journal of Industrial Organisation*, Vol. 26, pp. 153-179.

Arundel A. (2001), "The relative effectiveness of patents and secrecy for appropriation", *Research Policy,* Vol. 30, pp. 611-624.

Baum, J.A.C. and B.S. Silverman (2004), "Picking winners or building them? Alliance, intellectual, and human capital as selection criteria in venture financing and performance of biotechnology start-ups", *Journal of Business Venturing*, Vol. 19, pp. 411–436.

Carbone, J., E.R. Gold, B. Sampat, S. Chandrasekharan, L. Knowles, M. Angrist and R. Cook-Deegan (2010), "DNA patents and diagnostics: not a pretty picture", *Nature Biotechnology*, Vol. 28, pp. 784-791.

Chang, M.C. and J.D. Keasling (2006), "Production of isoprenoid pharmaceuticals by engineered microbes", *Nature Chemical Biology*, Vol. 2, pp. 674–681.

Chesbrough, H.W. (2003), *Open Innovation: The New Imperative for Creating and Profiting from Technology*, Harvard Business School Press, Boston, MA.

Chesbrough, H.W. (2006), "Open innovation: a new paradigm for understanding industrial innovation", in H.W. Chesbrough, W. Vanhaverbeke and J. West (eds.), *Open Innovation: Researching a New Paradigm*, Oxford University Press, Oxford and New York.

Committee for Economic Development (2012), "The future of taxpayer-funded research: who will control access to the results", CED, Washington, DC.

Correa, C.M. (2000), *Intellectual Property Rights, the WTO and Developing Countries: The TRIPS Agreement and Policy Options*, Penang, Zed Books and Third World Network, London and New York.

Dahlander, L. and D.M. Gann (2010), "How open is innovation?", *Research Policy*, Vol. 39, pp. 699-709.

Ebers, M. and W.W. Powell (2007), "Biotechnology: Its origins, organization, and outputs", *Research Policy*, Vol. 36, pp. 433–437.

ETC (2007), "Extreme genetic engineering: an introduction to synthetic biology", www.etcgroup.org/es/node/602.

Greenhalgh, C. and M. Rogers (2010), *Innovation, intellectual property, and economic growth*, Princeton University Press, Princeton, NJ.

Hall, B. and R. Ziedonis (2001), "The effects of strengthening patent rights on firms engaged in cumulative innovation: insights from the semiconductor industry", in *Entrepreneurial Inputs and Outcomes: New Studies of Entrepreneurship in the United States*, G. Libecap (ed.), Elsevier, Amsterdam.

Henkel, J. and S.M. Maurer (2007), "The economics of synthetic biology", *Molecular Systems Biology,* Vol. 3, pp. 117-121.

Johnson, R. (2009), "Synthetic biology: challenges of ownership, access & rights", presentation at "Opportunities and challenges in the emerging field of synthetic biology", Washington, DC, 9-10 July.

Kumar, S. and Rai, A.K. (2007), "Synthetic biology: the intellectual property puzzle", *Texas Law Review*, Vol. 85, pp. 1745-1768.

Levin, R.C., A.K. Klevorick, R.R. Nelson and S.G. Winter (1987), "Appropriating the return from industrial R&D", *Brookings Papers on Economic Activity*, pp. 783–820.

NAS (2012), "Synthetic Biology for the Next Generation" symposium held on 12-13 June 2012, transcript from online video: http://events.tvworldwide.com/Events/IOM/NAS120612.aspx

OECD (2002), *Genetic inventions, licencing practices and intellectual property rights: evidence and policies*, OECD Publishing, Paris, www.oecd.org/sti/sci-tech/2491084.pdf.

OECD (2005), "Intellectual property and competition policy in the biotechnology industry", *OECD Policy Brief*, OECD Publishing: www.oecd.org/dataoecd/36/4/35040373.pdf.

Rutz, B. (2009, "Synthetic biology and patents: a European perspective". *EMBO Reports*, Vol. 10, Special Issue, pp. S14-S17.

So, A.D., N. Gupta, S.K. Brahmachari, I. Chopra, B. Munos et al. (2011), "Towards new business models for R&D for novel antibiotics", *Drug Resistance Updates*, Vol. 14, pp. 88–94.

Torrance, A.W. (2010), "Synthesizing law for synthetic biology", *Minnesota Journal of Law, Science and Technology*, Vol. 11, pp. 629-665.

Toyoda, T. (2011), "Methods for open innovation on a genome-design platform associating scientific, commercial, and educational communities in synthetic biology", *Methods in Enzymology*, Vol. 498, pp. 189-203.

WIPO (2011), "Patent-related flexibilities in the multilateral legal framework and their legislative implementation at the national and regional levels", Part II, CDIP/7/3, World Intellectual Property Organization, Geneva.

Zheng, Y., J. Liu and G. George (2010), "The dynamic impact of innovative capability and inter-firm network on firm valuation: A longitudinal study of biotechnology start-ups", *Journal of Business* Venturing, Vol. 25, pp. 593–609.

Zimmeren, E. van, S. Vanneste, G. Matthijs, W. Vanhaverbeke and G. Van Overwalle (2011), "Patent pools and clearinghouses in the life sciences", *Trends in Biotechnology*, Vol. 29, pp. 569-576.