THE INTELLECTUAL COMMONS AND PROPERTY IN SYNTHETIC BIOLOGY

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Abstract
Is the development of synthetic biology threatened by sharing and ownership issues? What measures are synthetic biologists taking to address intellectual property and commons issues that may threaten development of the field? Part I presents a conceptual framework for the analysis of ownership and sharing in emerging technologies, organized around two dimensions -- a private ownership vs commons axis and a clarity vs ambiguity axis. It then uses the framework to assess the fit between conventions governing intellectual property and elements of synthetic biology. Part II describes internal positions on ownership and sharing within the community of synthetic biologists, highlighting areas of agreement on common ownership of registries of parts for basic research and education, standards for performance and interoperability, and design and testing methods; and agreement on private ownership of designs of devices ripe for commercialization. Part II also discusses the varied views of synthetic biologists on precisely where to draw the line on public versus private ownership of biological parts and design principles. The conclusions examine domestic and international forces that may shape the evolution of formal legal conventions and informal practices in synthetic biology.

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1.1 INTRODUCTION: OWNING AND SHARING SYNTHETIC BIOLOGY

> The justification of the patent system is that by slowing down the diffusion of technical progress it ensures that there will be more progress to diffuse…. Since it is rooted in a contradiction, there can be no such thing as an ideally beneficial patent system, and it is bound to produce negative results in particular instances, impeding progress unnecessarily, even if its general effect is favorable on balance.
>
> Joan Robinson, *The Accumulation of Capital*, 1956

> Overly restrictive licensing and smotheringly broad patent interpretations could make a shambles of synthetic biology. Half a century ago if recklessness, greed and unreasonable fear had somehow handicapped the development of integrated circuits, then the computing and communications revolutions would have been snuffed out. Now is an equally pivotal moment for the future of biotechnology.
>
> "How to Kill Synthetic Biology," *Scientific American*, June 2006

The classic view on intellectual property rights, expressed by Joan Robinson, sets forth a tension between fostering innovation through private ownership and enabling diffusion of the fruits of innovation.[16] By contrast, the editors of *Scientific American* warn that property rights conventions grounded in that classic view may impede development of the synthetic biology, stunting innovation and limiting diffusion of the fruits of innovation.[17] Is the development of synthetic biology threatened by sharing and ownership issues? What measures are synthetic biologists taking to address intellectual property and commons issues that threaten development of the field? What constraints imposed by external forces may limit the sharing and ownership strategies of synthetic biologists?

In fact, synthetic biology may be exceptionally susceptible to what has been called the "anti-commons problem," where ambiguity in property rights deters innovations *and* limits the utilization of new discoveries, creating the worst of both worlds. Synthetic biologists are seeking to turn biology into an engineering discipline. Their focus is on creating biological components that may be readily assembled into devices with medical, energy, materials fabrication and computing applications. Modular biological parts, standards for assembly and performance, designs of assembled devices and systems, and the methods used to accomplish these ends are all potential objects of sharing and ownership. As a consequence, the enterprise of synthetic biology may be more vulnerable than most emerging technologies to disputes over intellectual property.

Part I presents a general conceptual framework for the analysis of ownership and sharing in emerging technologies, organized around two dimensions -- private ownership vs commons axis and clarity vs ambiguity. It then uses the general framework to assess the fit between *de jure* and *de facto* conventions governing intellectual commons and property and the elements of synthetic biology that are objects of ownership and sharing.

Part II describes positions on ownership and sharing within the community of synthetic biologists, highlighting areas of agreement on common ownership of infrastructure, including registries of parts for basic research and education, standards for performance and interoperability, and design and testing methods; and agreement on private ownership of designs of devices ripe for commercialization. Part II also discusses the varied views of synthetic biologists on precisely where to draw the line on public versus private ownership of parts and design principles.

The conclusion offers conjecture on the evolution of property rights issues that bear on synthetic biology. Ironically, as synthetic biology matures to commercial viability, the ability of synthetic biologists to maintain the commons on infrastructure and to defend unrestricted private protection of devices and some parts is likely to erode. Under Bayh-Dole, universities may limit sharing of increasingly valuable property by commons oriented academics, while international negotiations on heath and environment may compel private developers of climate change and health technologies to accept differential pricing and compulsory licensing by developing country users.

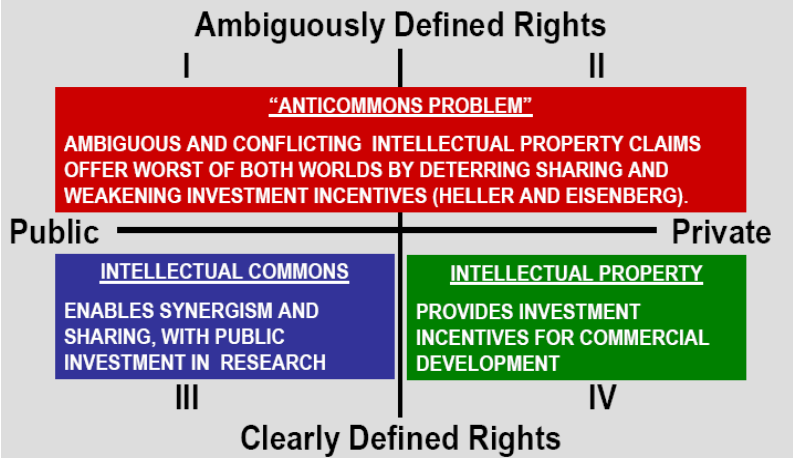
1.2 FRAMEWORK: SHARING, OWNERSHIP AND THE ANTICOMMONS

Synthetic biology sits uncomfortably within the intellectual property rights tradition of liberal market economies. To set up analysis of intellectual commons and property, consider the two dimensions presented in Figure 1. The horizontal axis separates public from private intellectual property ownership arrangements. The vertical axis moves up from clarity to ambiguity in the definition of property rights. In Boxes I and II, ambiguity begets an "anti-commons" problem that deters sharing and weakens investment incentives simultaneously. In Boxes III and IV, property rights are clearly defined, but ownership arrangements differ. In Box III, the intellectual commons fosters

intellectual synergism, but innovation may require public investment of economic resources. In Box IV, the intellectual enclosure of private ownership provides incentives for private investors but may impede sharing and collaboration. Where do synthetic biologists and the major elements of synthetic biology fall within these domains?

Synthetic biologists typically favor different intellectual property regimes for the different elements of synthetic biology. Most synthetic biologists agree that infrastructure including protocols, standards, registries, design methods, and testing methods should be located in the commons of Box III. Most synthetic biologists believe that commercializable devices composed of biological parts should be located in the private enclosures of Box IV. Synthetic biologists divide over whether ownership of biological parts should fall in the commons of Box III or the private domain of Box IV, with varying views on which ownership regime will promote faster development, diffusion, and commercialization of synthetic biology and with varying views on how to balance private and public economic interests. Finally, virtually all synthetic biologists view Boxes I and II as a threat to development of the field, and favor measures to reduce ambiguity, enhance clarity and reduce transaction costs to escape the anticommons. Let us consider each of these cells and the fit with elements of synthetic biology.

FIGURE 1: A FRAMEWORK FOR ANALYSIS OF INTELLECTUAL COMMONS AND PROPERTY



1.2.1 THE ANTICOMMONS: AMBIGUITY IN SHARING AND OWNERSHIP

Whether the assigned owner of intellectual property is a private or a public entity, the less clearly ownership is defined the more both innovation and diffusion are impeded. Ambiguity, confusion, and clutter in the definition of intellectual property rights are at the heart of what Heller and Eisenberg have called the "anti-commons" problem. Complex, interlocking, and ambiguous claims have the potential to create a worst-of-all worlds, deterring investment and impeding intellectual synergism simultaneously.[1] Consider a domain where ambiguous property rights claims make it difficult for potential innovators to know what has been discovered, what discoveries might infringe on existing claims, and with whom an innovator should contract so as to legally use the discoveries of others. How could a potential innovator do basic research? How could that innovator hope to commercialize innovations? A lack of clarity in property rights claims and broad preexisting claims may reduce innovation by impeding basic research and by deterring the investments needed to make use of discoveries.[2] As broad patents are awarded, potential innovators risk stepping on an increasing number of upstream claims across various scientific fields; are forced to engage larger and more expensive legal teams to consider the property rights implications of

[1] Heller and Eisenberg argue that research rights on patents set biomedical technologies apart from information technologies which tends to be characterized by other forms of property rights, including copyright, and "work-around" solutions. [4]

[2] Note that the number of players involved in ambiguous public ownership world could be one (the national government) or many (public universities, government agencies, and others). The number of players in an ambiguous private ownership situation could be one (IBM in the 1980s, which owned hundreds of key information technology patents) or many (small biotech firms each banking on a small intellectual property ownership portfolio). Though costs and types of transactions in each situation differ, ambiguity leads to suboptimal results in all.

research and development choices; and lean away from projects altogether if these costs prove too high. In particular, uncertain claims on upstream foundational research can be particularly harmful to downstream commercial applications. When the patent landscape is complex, claims are ambiguous, and potentially enforceable rights are present both upstream and downstream, and "reach-through" costs for downstream actors increase. Actors in such situations must figure out which of many upstream properties may "reach-through" and require licensing. As the ambiguity of rights increases, so too does the risk of a "submarine" patent owner making claims in the wake of a commercial success and incurring costly litigation. Such patent owners, or "patent trolls," may purposely or inadvertently wait to reveal and enforce claims until follow-on innovators have made lucrative discoveries. Though large firms can perhaps afford the *ex post facto* risk of payouts to litigants, smaller innovators in emerging fields like synthetic biology may be deterred by the expected costs that litigation imposes on successful downstream research. Ambiguous protections of biological intellectual property may be caused by technical complexity, a lack of familiarity with emerging biotechnologies, ethical and moral issues, and international divergence.

What specific faces do anti-commons problems present in the field of synthetic biology? Many patents in biological technology present overly broad and ambiguous claims that can contribute to the anti-commons. In our first example, a biological engineer would like to develop biological chassis that can count the number of times a cell divides to build in a timed self-destruction switch to limit survivability in the event of uncontrolled release. Obtaining resources to conduct such work may be inhibited by the existence of US Patent 6,774,222 on "Molecular Computing Elements, Gates and Flip Flops," a broad patent assigned to Schneider *et al* in 2004 with claims that have not yet been tested in court. Joining the preexisting notion of gates and flip flop circuits with the preexisting notion of biological systems is, in our view, an obvious combination of elements of preexisting art. By awarding tis patent, the US Patent and Trademark office is forcing anyone working in the very broad field of biological to license the right to do the obvious.

Our second example elicited much consternation among participants at SB4.0, the 2008 international synthetic biology meeting in Hong Kong. The firm Synthetic Genomics filed two US patent applications that could be interpreted to cover much of the field of synthetic biology as a whole. US Patent Application 2007264688 on "Synthetic Genomics," filed by Venter *et al* in 2007, sets forth extraordinary broad claims with respect to methods for constructing a synthetic genome. If granted, the patent would create an upstream problem for most significant work in synthetic biology. US Patent Application 20070269862 on "Installation of Genomes or Partial Genomes into Cells or Cell-like Systems," was filed by Glass *et al* in 2007. It covers methods of introducing a genome into a cell or cell like system, with extraordinarily broad claims covering the production of medicines and biofuels. If granted, biological engineers developing methods of biofuels production through implantation of synthetic pathways in re-engineered e.coli and yeast would be in trouble. It is our view that these applications should be and will be rejected or substantially narrowed on the basis of the existence of prior art. For example, the Glass application should run afoul of Keasling's existing patent on "Biosynthesis of Isopentenyl Pyrophosphate." Keasling's patent describes methods of introducing into host microorganisms pathways with sequences necessary for converting intermediates into isopentenyl pyrophosphate. The Keasling patent with its narrower and more specific description and more circumscribed claims has important direct implications for production of drugs and biofuels and has generated significant foundation, venture firm, and public funding. The Glass application fits within a time honored tradition of filing the broadest possible patent applications with an expansive set of claims. What are the risks to development of the field associated with the patenting strategy followed by Synthetic Genomics? Practitioners fear that patent examiners with limited experience in the emerging field of synthetic biology may fail to pare down claims advanced in these applications to appropriate size or to reject them outright.[3] And even if patent applications on "Synthetic Genomics" and on "Installation of Genomes" are ultimately rejected, such aggressive patenting application strategies have detrimental effects on the development of the field. The existence of the applications, the inordinate length of time that the patent system takes to provide clarity, and the possibility that these patents may be granted while the patent systems grinds along inhibit investment and raise transaction costs, particularly for small innovative firms.

To address the "anti-commons" problem, synthetic biologists are considering a range of options. Some are challenging existing anti-commons exacerbating patents on grounds such as obviousness or infringement on prior art. Requesting reexamination is time-intensive, costly, complex, and ultimately works best in the context of a test case. But the Public Patent Foundation, a growing public advocacy group, has successfully challenged a number of biotechnology-related patents via reexaminations, though not yet in the field of synthetic biology.[13] Similarly,

[3] The US Supreme Court ruling in *KSR* v. *Teleflex*, 550 U.S. 398 (2007) and the US Court of Appeals for the Federal Circuit ruling in Bilski 2007-1130 (Serial No. 08/833,892) may reduce the likelihood that broad patents that combine obvious elements of prior art will be granted in the future.

patent applications can be challenged before examiners make a decision. This process is still relatively time-intensive and complex. Because the benefits of challenging patent applications are diffuse while costs are concentrated, collective action in the form of pre-issuance challenges is likely to be underprovided. But new initiatives outside the synthetic biology community, such as The Peer to Patent Project [12], attempt to leverage the Internet in order to reduce both the costs and hassle of challenging patent applications. Additionally, search tools like Patent Lens sponsored by CAMBIA, a non-profit biotech research organization, allow researchers to efficiently monitor new patent application activity around specific search terms and even genetic sequences.[11] Synthetic biologists, including graduate students at MIT and groups in Europe and Australia, have organized "patent goon squads" to monitor patent application activity in synthetic biology. If these collaborative efforts can effectively surmount the collective action problems inherent to patent reform, their success could help reduce clutter and minimize the "anti-commons" problem.

1.2.2 PUBLIC SHARING VERSUS PRIVATE OWNERSHIP

If and when property rights are clearly defined, should they be assigned to public or private owners? Let us turn from "anti-commons" issues to the horizontal axis of Figure 1. Intellectual property rights are intended to protect new, useful, and non-obvious products of a creator's intellectual efforts. In the US Constitution, the rationale is that only by offering non-ambiguous protection to innovators can governments ''promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." Innovation is fostered by assigning private property protections and creating investment incentives. Patents and other private intellectual property protections thus trade off constraints on social welfare caused by granting time limited monopolies, with the incentives such monopolies provide for investment of time, money, and energy in invention. Joan Robinson and other advocates of this view implicitly assumes that without private intellectual property protection, innovation will be at sub-optimal levels, as inventors would not otherwise be able to recoup the costs of innovation.

Can intellectual property regimes be designed to hit a sweet spot between promotion of innovation and the rapid diffusion of technology? The problem with too much intellectual property protection is that innovation will stagnate at sub-optimal levels; the pursuit of innovation would be deterred by existing protections of property rights. Why innovate if it is more profitable to exploit existing intellectual property claims or to do something else entirely? Too many or too lengthy time limited monopolies can produce socially negative results if they result in less, rather than more, progress to diffuse. Arti Rai and James Boyle of Duke University Law School argue that the existence of private intellectual property protection can result in stagnation and that an intellectual commons may in some cases result in more innovation.[14] This would be true if the benefits of synergism provided by an intellectual commons are better able to create "more progress to diffuse" than Robinson's traditional patent system. In a commons, scientific and technical collaboration would not be hampered by the legal transaction costs incurred in licensing patents, and barriers to entry of new practitioners would be lowered. An intellectual commons has the potential to allow practitioners to share information and ideas in a manner that spurs new levels of innovation. Further, advocates of the intellectual commons suggest that first-mover advantages to early innovators rather than traditional property rights protections may provide sufficient incentive to spur investments needed for technological progress.

There is broad agreement within the community of synthetic biologists that developing an intellectual commons is necessary to promote basic research and education. Fostering a new generation of synthetic biologists through educational efforts and developing foundational knowledge through basic research are vital to the advancement of the field. Despite "anti-commons" concerns and the precariousness of the intellectual property/commons tradeoff discussed in the section above, basic research and education is thriving not only in synthetic biology but across all scientific fields. Academics are generally protected by *de jure* or *de facto* research exemptions on intellectual property, which allow basic researchers and educators to use otherwise protected intellectual property. These formal research exemptions are common in advanced industrial countries in Europe and Asia and are all but universal in developing countries. The United States, however, is notable for its lack of a formal research and education exemption, with reliance on informal norms that leave educators and academic researchers in some legal peril. We discuss below the standard European research exemptions, the state of statutory research exemptions in some emerging markets, Belgium's very broad research exemption, and the statutory narrowness and de facto informality of the US exemption.

In some countries, research exemptions stipulate that researchers must be non-profit, non-commercial, and/or part of an academic institution in order to qualify. Beyond such stipulations, research exemptions generally take into account research "on" a protected piece of property and sometimes research "with" a protected piece of property. Research "on" an item would entail, say, a researcher testing the properties and usefulness of a patented

molecule. If the researcher finds the molecule interesting and wants to use it, then the researcher would go about licensing the molecule. If not, no licensing agreements need be made. Research "with" an item indicates that the ultimate goal of the research is to understand something external to the protected property itself. For example, a researcher might incorporate a molecule in a larger drug delivery system. Should the researcher decide to develop this system, IP licensing agreements would be made. If unsuccessful, a "with" exemption protects this kind of research that experiments with protected property.

Standard Advanced Industrial Country Position Exempting Research On: The standard set by the European Union (Directive 98/44/EC) allows researchers to be exempt from standard intellectual property rights rules when doing research "on" a protected item, but not using, or "with," that item. The rationale behind this is that an "on" protection enables basic research while still affording protection to research tools and processes which could only be used in the context of "with" (like an innovative microscope). Australia, Austria, Canada, France, Germany, Iceland, Israel, Japan, the Netherlands, New Zealand, Norway, Switzerland and the UK are among countries with research exemptions on protected property.

Standard Developing Country Position Exempting Research On and With: In most developing countries, exemptions protect research done both "on" and "with" a piece of protected property. As Table 1 indicates, developing countries such as Mexico, Turkey, China and India and newly industrializing countries like Korea include sweeping research exemptions in their statutes. While the precise meaning and enforcement of these exemptions are generally untested, they fit with a developmental mindset that it is in a country's best interests to facilitate research which has the potential to expand into innovative and profitable applications, to improve the quality of education offered in a country, and to contribute to provision of well trained human capital to be an attractive environment for firms. On the other hand, trade officials from the US and Europe see these broad exemptions as examples of developing countries legalizing and encouraging the appropriation of protected intellectual property.

Belgium as Permissive Outlier Exempting Research On and With: Belgium an advanced industrial country with an exceptionally permissive research exemption. A struggle over the legal protection of biotechnological inventions resulted in expansion of the research exemption and a compulsory licensing mechanism for public health. The inclusion of "on" and "with" exemptions was intended to eliminate uncertainty and to guarantee "maximum freedom to operate" for research activities.[4] The statute is a signal to scientific and technological researchers, in both universities and firms, that Belgium welcomes innovative basic research. The statue also implies that Belgium expects the benefits of promoting basic research to outweigh the costs that might arise from commercial firms and researchers unhappy with the lack of IP protection for research "with" their protected properties. It is worth watching whether this policy proves successful, with potential influence on EU standards.

United States as Restrictive Outlier with No Exemption: The US is also an outlier among advanced industrial nations in Table 2, with no"on" or "with" exemption.[5] The Federal Circuit ruled in Roche v Bolar that the research exemption is limited to experiments "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry," and that experimental use does not allow "a violation of patent laws in the guise of 'scientific inquiry' when that inquiry has…not insubstantial commercial purposes."[6] Madey v Duke University further reinforced this limited research exemption in 2002.[7] The National Research Council advises that a "reasonable interpretation" of Madey v Duke is that "formal research enjoys no absolute protection from infringement liability regardless of the institutional venue, the purpose of the inquiry, the origin of the patented inventions, or the use that is made of them."[8] At present, synthetic biology is anchored in the one major country without a formal fundamental research and education exemption. How does the peculiar US legal-technical system function in practice?

First, in both academic and commercial worlds, US researchers often perform preliminary analyses on or with protected property to determine whether further research would be useful. The right of academics and firms to do preliminary research using protected property, without profiting directly, is accepted informally. In a world where businesses rely on academic discovery and where academics have long term relations with private firms, it is generally not a good investment of time, money, or goodwill to enforce property claims against education or basic

4 Van Overwalle, van Zimmeren [18] suggest that compulsory licensing for public health, allowed under the WTO TRIPS Agreement, has given rise to more debate than the research exemption.

[5] The US has relatively clear statutes allowing firms submitting generic drugs to the FDA to benefit from the already proven quality of branded drugs protected under patents. This exemption for regulatory approval is meant to facilitate the quicker diffusion of generic drugs following the expiration of the branded patent.

[6] Roche Products Inc v Bolar Pharmaceutical Co 733 F 2d 858 (Fed. Cir. 1984)

[7] Madey v Duke University 307 F 3d 1351, 1362 (Fed. Cir. 2002)

[8] National Research Council (2004) as quoted in [2]

research. Commercial and academic players in the synthetic biology community are skeptical that property rights claims against academics would ever be enforced for these reasons.

TABLE 1: COUNTRIES WITH EXCEPTIONAL RESEARCH EXEMPTIONS[9]

Country	Scope of Exemption	Origins	Content
Belgium	Explicitly protects research "on" and research "with"	Amending Act Article 11 (2005), to the Belgian Patent Act (1984)	Research exemption covers research performed either on or with a patented invention, for mixed scientific and commercial purposes. Specifically widened to fix uncertainty regarding the on/with distinction in the EU directive.
China	Wide exemption for any experimental or research use	Patent Law, Article 62(5) (2004)	"...where any person uses the patent concerned solely for the purposes of scientific research and experiment."
Korea	Wide exemption for any experimental or research use	Patent Law, Section 91(1)	"The effects of the patent right shall not extend…to the working of the patented invention for the purpose of research or experiment…"
India	Wide exemption for any experimental or research use	Patents Act, Section 47(3) (1970)	"...any process ... may be used ... for the purpose of merely experiment or research...."
Mexico	Research "on" and "with" if non-commercial, in either private or academic sphere	Industrial Property Law, Article 22 (1994)	"The right conferred by a patent shall not have any effect against…a third party who, in the private or academic sphere and for non-commercial purposes, engages in scientific or technological research activities for purely experimental, testing or teaching purposes, and to that end manufactures or uses a product or a process identical to the one patented."
Turkey	Wide exemption for any experimental or research use	Patents Decree Law, Section 75 (1995)	"The following acts shall remain outside the scope of the rights conferred by the patent…acts involving the use of the patented invention for experimental purposes…"
United States	Unclear protection of research "on"; no special status for universities or non-profits	Case law: Roche Products v Bolar Pharmaceutical (1984) and Madey v Duke University (2002); Merck KGaA v. Integra Lifesciences, 545 US 193 (2005)	Statutory exemption extends to all uses of patented inventions that are on the path to FDA submission (meaning generic drugs). Experimental use is limited to experiments "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry." Some confirmation of freedom to use the invention for R&D work prior to the time the product begins to be commercialized.

Second, legal uncertainty in the US creates a difficult situation for third party researchers who may unwittingly infringe on property rights when facilitating exchange among basic researchers and educators. The Registry of Standard Biological Parts and other registries of biological components may face this problem. In the absence of a US research exemption, scientists, university technology transfer offices, and private organizations have developed consortial arrangements to encourage patent pooling and sharing. By involving the private sector as well as academia, such strategies increase awareness of the research exemption problem while at the same time establishing partial workarounds and thereby expand and codify the basic research exemptions without changing statutes. But a clear research exemption would protect those involved in providing biological components to other researchers for basic research and education.

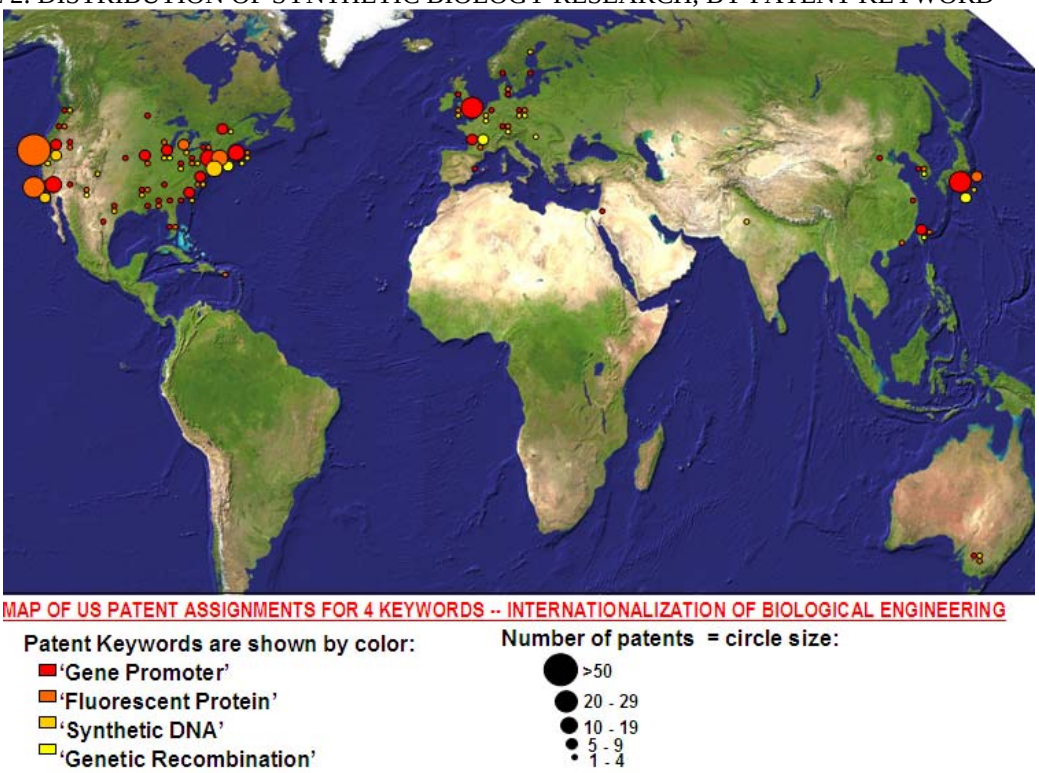
Third, parts registries may be expected to expand in countries with permissive exemptions. Academic researchers in general have the option to exploit regulatory differences in order to facilitate current research. In accounting regulation, for example, Sarbanes-Oxley legislationhas spurred initial public offerings on non-American

[9] Assembled by the authors from statutes and news articles. Information on OECD countries from [2] and [10].

stock markets like the London Stock Exchange. An analogous relocation of activity to avoid onerous or ambiguous regulation could happen in synthetic biology.

Finally, relocation of activities could also make visible the opportunity costs of what seems an untenable American position on exemption of basic research and education. Indeed, as Figure 2 indicates, synthetic biology is already an international discipline.[10] Although this figure underestimates synthetic biology research worldwide, it nevertheless indicates that research in synthetic biology is not an American-only enterprise. With relocation of research in response to regulatory differences and with increasing pressure for international intellectual property rights harmonization, it is unlikely that research exemptions will continue to vary across advanced industrial nations over the long term. As the single major outlier, the US is likely to bring US statutes into line with US informal practices and with the statutes of Europe, Oceania and Japan.

FIGURE 2: DISTRIBUTION OF SYNTHETIC BIOLOGY RESEARCH, BY PATENT KEYWORD[11]



1.3 OUTLOOK: PERSPECTIVES FROM SYNTHETIC BIOLOGISTS

Synthetic biologists have varied views on ownership and sharing. There is widely shared agreement on the need for common ownership of infrastructure, including registries of parts for basic research and education, standards for performance and interoperability, and design and testing methods. There is variation in views of synthetic biologists precisely where to draw the line on public versus private ownership of parts and design principles. There is widely shared agreement on the advantages of private ownership of designs of devices ripe for commercialization. Additionally, practitioners agree that the commercialization of complex biological systems requires patenting to

[10] This figure was created by searching US and European patent databases for selected keyword phrases common to synthetic biology. Current research aims at creating a more comprehensive database of keyword phrases in synthetic biology that will be able to provide a more complete picture of the existing "patent landscape". In addition to the MIT SynBERC group's work on this patent landscape, a consortium of social scientists present at Synthetic Biology 3.0 as well as other European groups are doing complementary work.

[11] Thanks to Hanna Breetz and Matthew Silver for the research and assembly of this data as of 2007. Note that this map should be taken only as indicative of research in the field as a whole. Research teams at Lancaster University, the Technical University of Munich, and elsewhere are constructing more authoritative patent landscapes.

incentivize firms to undertake initial investments. Thus, aspects of traditional intellectual property rights and an intellectual commons both have roles to play in synthetic biology, though the line as to where the commons should end and private property begin remain points of controversy in the synthetic biology community.

TABLE 2: PERSPECTIVES ON COMMONS AND PROPERTY WITHIN THE SYNBIO COMMUNITY

	Biobricks Foundation Commons Advocates Favor	SynBIO Firms Property Advocates Favor	Summary of US Law
INFRASTRUCTURE			
Registry of Parts	Public Research and Education Exemption	Varies across registries and purposes	US no exemption Exemptions vary abroad
Standards			
* Interoperability	Public Domain	Public Domain	Ownable
* Performance	Public Domain	Public Domain	Ownable
Methods			
* Design tools	Public Domain	Public Domain	Ownable
* Testing methods	Public Domain	Public Domain	Ownable
BIOLOGICAL PARTS			
* Fragment of DNA	Public Domain	Public Domain	Not ownable
* With useful function	Public Domain	Private Property	International variation
* Performance data	Public Domain	Conditional	Ownable
* Redesigned chassis	Public Domain	Public Domain	Ownable

Table 2 summarizes the positions of synthetic biology commons and property advocates regarding what we call "infrastructure" and biological parts. There is substantial agreement between the two camps regarding the ideal ownership status of standards and methods in synthetic biology. Interoperability, performance measures, design tools, and testing methods are central to the design and re-design of biological systems in systematic ways. Many commons and property advocates agree that an ownership scheme that situates these in the public domain is best for the development of synthetic biology. If proprietary standards were cheaply licensable, commons-type goals could be achieved under private ownership; some practitioners cite Invitrogen's Gateway system as a good example of popular and easily available proprietary standards. But in the absence of public domain standards, there still remains the opportunity for IP holders to compartmentalize what many practitioners would rather see as immediately available and universal standards upon which mutually intelligible research could take place.

While both commons and property advocates see the intellectual commons of the Registry of Standard Biological Parts as important to education and training, there is some disagreement over how practitioners with interests in academic advancement and/or commercializing innovations should participate in the Registry. Open-source proponents disagree with what they describe as the biological sciences' modus operandi of "patent early and often" to garner both academic kudos and potential commercial profits. Yet whether incentives can be designed to encourage practitioners to contribute their best work to a synthetic biology intellectual commons remains an open question. Graduate students, post-doctoral students, and professors, not to mention commercial practitioners, traditionally rely on their invention and/or ownership claims for individual career advancement. To the extent that submitting research to, say, the Registry of Standard Biological Parts undermines a practitioner's ability to publish a scientific paper or to otherwise benefit from her investment in research, intellectual commons-based synthetic biology will remain a challenging norm to establish. Some practitioners resolve this conflict by indicating their willingness to contribute research to common-pool resources like the Registry of Standard Biological Parts but only after key publications and/or patents have been acquired. Others who advocate the growth of common-pool resources see this compromise as insufficient since the delay between discovery and the ability of others to license, let alone freely use, new biological components undermines the idea of creating a common toolkit from which to build standardized and interchangeable biological systems.

Disagreement over the patenting of biological parts centers on whether or not private property is necessary to spur innovation and commercial interest in synthetic biology. There is relatively broad agreement that, because a complex biological system is a "downstream" application of various elements of "upstream" basic research, such a system could and should be covered by a patent without deterring "upstream" research. And the common ownership of the most "upstream" aspect of synthetic biology, DNA fragments, has already been addressed by patent offices. A

December 1999 change by the US Patent and Trademark Office requires that inventions have both "specific and substantial" utility, preventing the IP protection of DNA fragments without specification of useful functions.[12] Commons advocates compare patent protections on individual biological parts with useful functions and performance data on those parts as analogous to the problem with patenting DNA. Parts with functions like signaling, counting, promoting, etc. would necessarily be underutilized were they protected by individual patents. Additionally, commons proponents note that the expense and time required to license thousands of individual biological parts is prohibitive, especially as biological systems move from including tens to hundreds of unique modular biological parts.

Intellectual property advocates, on the other hand, seek to preserve incentives for researchers to do the work in assembling and characterizing biological parts. There is broad agreement that the information on many parts in the Registry of Standard Biological Parts has not been adequately screened, and that curators ensuring quality control are needed. Private intellectual property advocates attribute this to the lack of incentive for practitioners to properly describe and codify their research. If the benefits of proper performance data are diffused across the whole pool of synthetic biology practitioners, it is unsurprising that practitioners either free ride on others' altruism or come to expect the common-pool Registry of Standard Biological Parts to be of little use.

As Table 2 indicates, most of the elements of synthetic biology infrastructure and aspects of biological parts are currently "ownable" under US and international law. Nevertheless, there is a substantial and growing intellectual commons, particularly in academia among both professors and students, among practitioners who come from an information technology / open-source background and among some start-up biotechnology firms. Regardless of de jure legal provisions, the agreement of both commons and property advocates on public domain ownership schemes in aspects of infrastructure and private ownership in aspects of biological parts has contributed to the field's progress. Much like the formally absent but informally robust research exemption in American academia, the informal, community norms of synthetic biologists have sparked some amount of intellectual commons beyond even the minimum agreed upon by the community as a whole. However, the community at the present is moving away from some of the more radical views of commons advocates and toward advocates of standard patent protections on not only commercializable, complex systems but also on individual parts and performance data.

Synthetic biologists have been unified in promoting development of an international intellectual commons. For example, by 2008 the International Genetically Engineered Machine competition (iGEM) grew to include 84 teams representing 21 countries. The rapid growth in international participation in the iGEM competition is a testament to synthetic biologists' efforts to foster an intellectual commons worldwide. University and high school students use existing and design new standardized biological parts to build biological systems and operate them in living cells.[5] This competition is built around principles of openness and sharing, as many teams maintain Wiki pages describing their research and contribute newly designed parts to a central repository, the Registry of Standard Biological Parts [15]. The Registry ships parts to iGEM teams annually; it now makes available 700 biological parts and provides information on 1300 other parts and is hosted in a Wiki format which facilitates collaboration between iGEM students and professional synthetic biologists worldwide. Support for the iGEM competition and the Registry comes from across the synthetic biology community, providing the synthetic biology community with a prototypical example of a research and education oriented intellectual commons. Proponents of open-source synthetic biology actively participate in other intellectual commons sharing initiatives: they post ongoing research on the open wetware public domain site[9]; use Creative Commons licensing schemes; and encourage open standards setting and the development of public use "biofab" parts manufacturers. The BioBricks Foundation[1] is a not-for-profit organization founded by engineers and scientists from MIT, Harvard, and UCSF with significant experience in both non-profit and commercial biotechnology research; its mission is to encourage the development and responsible use of technologies based on BioBrick™ standard DNA parts that encode basic biological functions. The BioBricks Foundation advocates for community technical and legal standards and is the civil society group which best represents those advocating the broadest intellectual commons possible in synthetic biology.

1.4 CONCLUSIONS: THE FUTURE OF OWNERSHIP AND SHARING

Synthetic biologists stand out in their efforts to shape formal legal conventions and informal practices on intellectual property to promote development of their field. While there are disagreements within the field over the

[12] The USPTO [17] notes "invention must have specific and substantial utility…Exclude throw-away, insubstantial, non-specific utility." These directives are consistent with case law, including: Brenner v. Manson 86 S.Ct. 1033, 383 U.S. 519, 16 L.Ed.2d 69, 148 U.S.P.Q. 689 U.S.Cust. & Pat.App. March 21, 1966.

appropriateness of patenting biological parts, there is broad agreement within the field that commercializable devices are and should be patentable and that basic research and education and the infrastructure of technical standards, parts registries, and design methods should be treated as part of the intellectual commons.

How are formal legal standards and informal practices that govern sharing and owning likely to evolve? As the field of synthetic biology matures, applications to cellulosic biofuels, pharmaceuticals, exotic materials creation, and biological computing will become commercially viable with wide ranging economic, environmental, health and security effects. Arrangements for sharing and owning will evolve as applications of the field emerge and take on commercial value.

First, over the short term, academic synthetic biologists that favor commons oriented approaches to infrastructure development may be increasingly constrained by university technology licensing offices operating under the 1980 Bayh-Dole Act. With greater commercial viability of synthetic biology, individual synthetic biologists are likely to find technology licensing offices of their university imposing limits on their ability to contribute valuable inventions to the creative commons. The Bayh-Dole act allows universities to secure title to the products of invention created with public funding.[13] Even when inventions do not have immediate commercial value, university technology licensing offices often patent and license. For example, synthetic biologist Adam Arkin is listed along with McAdams as an inventor on US patent 5,914,891, titled "System and Method for Simulating Operation of Biochemical Systems." Arkin notes that he was pressured to apply for the patent by Stanford University, a patent that he calls "an example of an outrageously broad IPR claim…it is wrong."[14] As the parts, methods, and design principles that constitute synthetic biology take on significant commercial value, conflict between technology licensing offices wishing to privatize intellectual property and researchers seeking to strengthen the intellectual commons will only increase.

Second, over the medium term, with synthetic biology playing an increasingly prominent role in creation of second and third generation biofuels, commons and property issues are likely to fuse with debates over climate change and development. At UN Climate Change Conferences in Bali in 2007 and Poznan in 2008, the transfer of critical climate change technologies from advanced industrial countries to developing countries was a focal point for discussion. Assessments of potential barriers to transfer of renewable energy technologies to developing countries highlight "second generation biofuel technologies where methods, or enzymes, or new microorganisms for breaking down lignin are likely to be patented" as an area of special concern.[15] The experience of companies producing pharmaceuticals suggests that demands for formal compulsory licensing and informal appropriation of synthetic biology technologies for domestic use may be expected. The G77 plus China have already called for placing climate change technologies into the public domain, while academics including Jeffrey Sachs have called for loosening the terms of licensing. Members of the G77 plus China also call for endogenous technology development within developing countries as critical to addressing the problem of climate change. Synthetic biologists may wish to consider now how they will respond to intensifying demands by developing countries for freer access to climate change and health related technologies, perhaps by setting forth proposals with provisions for patent pooling and for differential pricing in technology licensing. Synthetic biologists may wish to move ahead of the curve on international intellectual commons and property issues, as they have in the development of other aspects of their field.

Third, over the long term, the G77 appeal for development of endogenous technical capabilities is being partially met by proactive measures including iGEM and the series of international conferences including holding SB4.0 in Hong Kong with heavy participation by teams from developing countries. iGEM and other outreach activities of synthetic biologists are models of how to transfer know how by building vibrant international science commons. The community of academic synthetic biologists has been working to accelerate the international diffusion and development of the field of synthetic biology by promoting development of endogenous capabilities abroad. Taken in conjunction with increasing commercial viability of technologies, continuing international diffusion of synthetic biology technologies will lessen the ability of the US government and US academics to shape

[13] There remains a legal restriction that the IP must not "diminish or detract from" the specific federally funded research goals or, if wholly tangential to the purpose of federal funding, it must be "without interference with or cost to the government-funded project." But interference or diminishment is difficult to prove, and thus these limitations are largely unenforced.

[14] Discussion with Adam Arkin, SB 2.0, Berkeley, California, 20 May 2006.

[15] See Burton [6] and WIPO [19] for moderate analyses on this issue. Intense concern over access to second generation biofuel patents were raised by China, India, Brazil and Korea delegates after the AWG-LCA Workshop on Research and Development of Technology, UN Climate Change Conference, Poznan 6 December 2008.

development of research, education, and sharing and ownership conventions. In practice, this suggests that a more commons oriented international property rights environment is likely to evolve.

As surely as night follows day, the evolution of synthetic biology from basic research and education to viable commercial production will transform arrangements for commons and sharing. The maturation and commercialization of the field will have mixed effects, with university technology licensing offices imposing limits on the ability of individual researchers to contribute generously to the commons, with international negotiations threatening appropriation of valuable assets compelling generosity, and with the diffusion of the methods and practices of synthetic biology ultimately relieving synthetic biologists in the US and Europe of the power and the responsibility for making choices on sharing and ownership. Paradoxically, as synthetic biology becomes commercially viable, the ability of synthetic biologists to defend unrestricted private protection of devices and some parts and to maintain the commons on infrastructure may be eroded.

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