Ownership, sharing and community-building in synthetic biology

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Boundaries

- The importance of social norms, values and organisational arrangements in intellectual property:
  - Extends the bounds of what is normally included in technical discussions of this topic

- Synthetic biology can change the nature of biological entities:
  - Pushes at the boundaries of the patent system
Aims

• To throw light on the interconnections between intellectual property norms, open source aspirations, and the dream of engineering biology

• To show how this is linked to a normative and community-building agenda in synthetic biology
What is synthetic biology?
“The design and construction of new biological parts, devices, and systems and the re-design of existing, natural biological systems for useful purposes” (www.syntheticbiotechnology.org)
Different schools of synthetic biology

- BioBricks approaches
- Genome-level work
- Protocell creation

O’Malley et al. (2008)
Making biology into an engineering discipline

Synthetic biology: new engineering rules for an emerging discipline

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A partnership between biology and engineering

Roger Brent
Engineering principles
Modularity in synthetic biology
Welcome to the Registry of Standard Biological Parts.

The Registry is a collection of ~3200 genetic parts that can be mixed and matched to build synthetic biology devices and systems. Founded in 2003 at MIT, the Registry is part of the Synthetic Biology community's efforts to make biology easier to engineer. It provides a resource of available genetic parts to iGEM teams and academic labs.

The Registry is based on the principle of "get some, give some". Registry users benefit from using the parts and information available from the Registry in designing their engineered biological systems. In exchange, the expectation is that Registry users will, in turn, contribute back information and data on existing parts and new parts that they make to grow and improve this community resource.

You’ll notice some significant changes to the Registry recently. In particular, the Registry catalog of parts has been entirely redesigned to allow for easier browsing of the available parts and devices. You can now browse parts and devices by type, by function, by chassis and by standard.

You’ll also notice that the documentation and help pages for each class of parts have been greatly enhanced.

The Registry of Standard Biological Parts is "always" a work in progress. Please browse the new catalog and let us know what you think, or feel free to edit and improve the pages further.

Registry news

- **June 22, 2009**: You can now link to part pages directly from the iGEM wiki by typing the following `<partinfo>Ba_B0015</partinfo>`.
- **June 11, 2009**: We are considering changing the license terms of the Registry so that we can share our information with other databases. Go here to read the proposal or add your comments.
- **June 2, 2009**: Most of the hard information about a part is now presented in the header and footer of the part's Main Page. In particular, the functional parameters and the categories for a part are presented in the footer. All of this information may be edited using the Edit button near the footer.
- **May 30, 2009**: For the convenience of software developers, the sequences and basic information about every part is available in FASTA format. Learn more here.
Modularity in synthetic biology

- Are biological systems actually made of functional modules?
- Or are they are simply best understood as such by the engineering approaches that are adopted in synthetic biology?
- “a human invention designed to assist people in engineering very complex systems by ignoring unnecessary details” (www.openwetware.org)?
- No consensus on this issue
Modularity in synthetic biology

- But even if natural systems aren’t modular, can they be made to be so?
Modularity and intellectual property

- Modular systems are not only easier to engineer, they are also well suited to intellectual property regimes.
- In applying engineering principles to biology, synthetic biology is making biology better fit IP.
- Modularity also “opens novel ways of imagining the organization of collaborative production” (Pottage 2009).
- Commons-based production and private appropriation rely on the very same ontological characteristics.
Synthetic genomics

(Gibson et al. 2010)
Synthetic genomics

• JCVI’s 2010 paper ‘Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome’ heralded as a landmark achievement
• Longer-term aim to develop a ‘chassis’ around which new life forms could be built
• Venter is notorious for vigorously pursuing IP
• He has ‘watermarked’ his name into the code of his synthetic bacteria

CRAIG VENTER
TTAATTACGCTAATGTCGTAATGGAGTAGAGAACACAGAACGATTAACTAGCTAA
Synthetic genomics

Illustration: Andrew Rae in *Wired* 15/09
Computational metaphors

- DNA sequencing “allows storage of the genetic instructions for life as a digital file” (Gibson et al. 2010)
- (Myriad ruling: DNA described as the “physical embodiment of biological information”)
- Explains why genes become the subject of patent applications
- But this down-plays the importance of cellular context (Kay 1999, Sarkar 1996, Barnes and Dupré 2008)
- The synthetic genome will only thrive if it is implanted into an existing cell
Ownership and sharing of BioBricks
Computational metaphors

• “DNA sequencing and synthesis technologies make genetic information and material interconvertible” (BioBrick Public Agreement presentation 2009)
• These technologies allow DNA sequences to be ‘decompiled’ and ‘recompiled’
“New organisms can be designed by combining short snippets of DNA—so-called standard biological parts—into complex genetic blueprints in the same manner that LINUX modules are now combined to make software” (Maurer 2009, p.806)
The BioBricks Foundation

- BioBricks Foundation has been set up in an attempt to ensure that the information needed to build BioBricks is freely available in the public domain.
- Aims to foster “the open design, construction, distribution, understanding, and use of BioBrick™ compatible parts” (BioBricks Public Agreement 2010).
- Synthetic creations are likely to require many BioBricks: patents could lead to patent thickets or blocking patents.
BioBrick Public Agreement

- Attempt to establish the grounds on which BioBricks can be accessed and shared, currently open for comments
- Sign-up would give access to all BioBricks in the Registry of Standard Biological Parts
- Contributors must promise not to assert any property rights they may hold on BioBricks
- Not ‘viral’, no share-alike clause
- Parts can be patented if they are in a mixed system, novel combination, or are inventive
- The aim is to enable a “rich, fully diverse ecology of commercial and public benefit “(BioBrick Public Agreement presentation 2009)
Diverse ecology

• Inspired by the rich ecosystem of software innovation
• Peer production of BioBricks is entirely compatible with more proprietary strategies (Pottage 2009)
• Alternative models, such as Henkel and Maurer’s (2009) ‘embedded Lunix’ have been proposed
• What are the norms, values and organisational structures that we see being co-constructed with the ownership and sharing regimes being developed in synthetic biology?
• These factors broaden the conversation into a wide range of topics beyond the bounds of patent law
• Two community-building efforts
Aim is to build a community which shares certain values about safety, security and open access.

Wants to shape “the ideology, values and culture of the synthetic biology community” (Smolke 2009).

Teams are rewarded for contributing parts to the Registry, and ‘debugging’ existing parts.

“engineering is not just a technical activity – it simultaneously builds norms and practices of collaboration into standardized parts” (Pottage 2009).

The technology and its social world are being created simultaneously.
IP and iGEM

- The competition is very successful, but rests on shaky IP foundations
- Many of the DNA sequences in the Registry are already covered by patent claims (Rai 2009)
- Strong IP on Green Fluorescent Protein
- The threat of litigation hovers in the background
- iGEM is breaking the existing IP regime: does this demonstrate that the IP regime is broken?
Users and hackers

• In software the distinction between developers and users is not sharp (Von Hippel 2005)
• If biology is becoming more like software, users can become more involved (biohacking)
• DIYBio is enabled by developments which have reduced the cost and increased the ease of access to technologies such as DNA synthesis
• Represents moves towards democratisation synthetic biology and a desire to make biology into a technology that is accessible to all
• Made up of: ‘biocurious’ amateurs (95%), artists, ‘moonlighting’ working scientists, bioentrepreneurs and a few “hacker culture uber libertarians” (Cowell 2010)
Motivations for commons-based approaches in synthetic biology

- Pragmatic: a commons-based regime can result in more innovation (Rai and Boyle 2007)
- Ideological: openness is adopted because it is considered the best way to “benefit the world” (BioBrick public agreement 2010)
- Strong ideological support for “the cause of radical openness” (Kelty 2005) in the synthetic biology community
- Aspirations that “the hacker culture values like elegant design, creativity and sharing beneficial works of engineering for all, will spread to biology” (Cohn 2005)
Motivations for commons-based approaches in synthetic biology

- Can address issues of equity, safety, responsibility and “broader acceptance” of the technology (BioBrick Public Agreement presentation 2009)
- In the future parents will be able to re-programme food, and children will design synthetic pets (Dyson 2007)
Broader social movements

- Open science: public domain, outside the IP system
- Open source: depends on pre-existing IP rights (e.g. copyleft)
- Open innovation: major global change in business models (Johnson 2009)
Open/distributed innovation

- Shift from the industrial economy to the knowledge economy
- Move away from centralised innovation
- More user-centred, aims to redistribute agency, knowledge and power
- We also see distributed user-centred innovation in areas like mountain biking and snowboarding (Von Hippel 2005)
Enlightenment 2.0: Unleashing the Open Science Revolution

Renowned physicist Freeman Dyson identifies two kinds of scientific revolutions, those driven by new concepts (theoretical), and those driven by new tools (technological).

In the last 500 years we’ve witnessed paradigm-shattering conceptual shifts associated with names such as Copernicus, Newton, Darwin, and, Einstein. Simultaneously, the evolution of technology drives progress in unpredictable ways—Galileo borrowed principles from the technology of eyeglasses to pioneer the use of the telescope in astronomy, while Watson and Crick relied on Rosalind Franklin’s skill with X-ray diffraction (a tool from physics) to probe the structure of life. (Undoubtedly, Franklin’s contribution would have been more fully recognized under a true Open Science Paradigm.)

To this classification of scientific revolutions, we can now add a third kind, an Organizational Revolution, the advent of a truly “Open Science,” which will profoundly affect the pace and character of subsequent theory and tool-driven paradigm shifts.

The 21st century is off to a rocky start, and as economic and ecological crises converge, there is no shortage of dire predictions. On the other hand, politicians and pundits point to the expectation that Science and Technology will let humanity invent its way out of the problems we’ve created. This rosy outlook ignores a deep crisis that has been brewing and could hamstring our innovative capacity when we most urgently need it.
Open/distributed innovation

- Open Science Summit aims for “a rapid, radical reboot of the global innovation system for a truly free and open 21st century knowledge economy”
- Moves towards openness are likely to have a disruptive affect on current business models
- Small companies could undermine existing platforms, displacing incumbent multinationals
- Where there is distributed innovation “there is a normative model of society being performed as well” (Rip et al. 2009)
Summary

• It is not feasible or helpful to try to separate out the legal, technical, social and political aspects of synthetic biology.

• Proponents of BioBricks admit that the engineering approach is a value system: some people reject it out of hand technically, others morally (Endy 2009).

• Can’t just study novel IP regimes in this field; we also have to be aware of the new social arrangements that are simultaneously being brought into being.
Summary

• The social and normative innovations being developed around BioBricks approaches rely on the ability to make biological entities into standardized modular parts
• But what if this technical aspiration is not successful?
The recalcitrance of biology
FIVE HARD TRUTHS FOR SYNTHETIC BIOLOGY

Can engineering approaches tame the complexity of living systems? Roberta Kwok explores five challenges for the field and how they might be resolved.

To read some accounts of synthetic biology, the ability to manipulate life seems restricted only by the imagination. Researchers might see entire programs to produce vast quantities of biofuel from renewable sources, or to increase the presence of humans or to release precise quantities of insulin as a body needs it — all visions inspired by the idea that biologists can extend genetic engineering to be more like the engineering of any hardware. The formula: Characterize the genetic sequences that perform needed functions, the parts, combine the parts into devices, and use them to achieve more complex functions, thus insert the devices into cells. As an all-but-true story, this chemistry could provide a toolbox for enabling genetic computation — biological versions of microprocessors and switches — to be plugged into cells at will.

But analogies don’t capture the daunting knowledge gap when it comes to how life works. However, “there are very few molecular operations that you understand in deep detail,” says Bethany Berbee, a principal at the engineering consulting and design company Biologic in Seattle, Washington. And as the diversity of networks gets larger, the ability to design more complex systems becomes more difficult. A 2010 report showed that although the number of published synthetic biological circuits has risen over the past few years, the complexity of those circuits — the number of biological parts they use — has begun to flatten.

Challenges begin at every step in the process, from the characterization of parts to the design and construction of systems. “There’s a lot of biology that gets in the way of the engineer,” says Christina Agapian, a graduate student doing synthetic biology research at Harvard Medical School in Boston, Massachusetts, but difficult biology is not enough to deter the field’s practitioners, who are already addressing the five key challenges.

Many are parts are undefined. A biological part can be anything from a DNA sequence that encodes a specific protein to a sequencing sequence that facilitates the expression of a gene. The problem is that many parts have not been characterized well. They haven’t always been tested to show exactly what they do, and even when they do, their performance can change with different cell types or under different lab conditions.

The Registry of Standard Biological Parts, which is housed at the Massachusetts Institute of Technology in Cambridge, for example, has more than 5,000 parts available to users, but does not guarantee their quality, says director Randy Rebagliatti, who has been at MIT since 2000. In 2004, 12 students used parts from a “kit” to develop new ways to design synthetic biological systems. But many of those system didn’t work in the past, partly because the design tools weren’t available.

To address this issue, a team of scientists from the University of Illinois at Urbana-Champaign is testing new tools for designing biological systems. “Our goal is to provide a more comprehensive toolkit for designing and testing parts,” says team member Adam Arkin, who is also a professor at the University of California, Berkeley.

THE PARTS' WORK LIKE LEGO

Imagines as these tiles in magazines or Wernier tosy synthetic biology as maps designed by Wernier tosy synthetic biology as maps designed and constructs. The parts that many of the potential parts are not well-characterized, or works practically in different configurations and conditions.
Scepticism about engineering biology

- Synthetic biologists pursuing BioBricks approaches are keenly aware of the difficulties
- They know that they are dealing with entities that reproduce and evolve
- It may be that modularity will not be successfully applied to biological entities
- If the engineering approach to biological systems is not successful, will the parallel with open source also fail?
- A large array of different players in the synthetic biology field, not all of whom embrace the open biology agenda
Diverse ecology or tipping point?

- Some synthetic biologists think we are moving towards a tipping point, where the field will either remain open, or the IP will be locked up.
- Powerful multinationals dominate the biotechnology field.
- Small synthetic biology companies require venture capital, and need to file patents to justify investment.
Pushing the boundaries of the biological

- Current biotech patenting regimes rest on certain ideas about the nature of biological entities
- Synthetic biology, if successful, could radically challenge these assumptions, because it has the ability to change biological entities
- The informational and software metaphors that are so widely drawn upon in the field could become actualised
- These metaphors are already changing what people believe should be patentable
- Biology is becoming more like software because we are making it more like software
- If synthetic biology succeeds will we have to rethink intellectual property protection in biotechnology?
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