

Biohackers

The Science, Politics, and Economics of Synthetic Biology

It has been said that if you ask five scientists for a definition of synthetic biology (often referred to as synbio), you'll get six different answers.¹ While it may frustrate policymakers, this semantics problem signifies synthetic biology's position as one of the most dynamic and misunderstood sectors of the life sciences today.

For the purposes of this paper, we define synthetic biology as the deliberate design and construction of a biological system to produce effects that would not ordinarily occur in nature. It is the process of combining raw DNA components into "synthesized" DNA strands that, when introduced into a living cell, create an organism that behaves according to the designer's intent. That could mean reprogramming the genome of a bacterium so that it manufactures a vaccine, engineering algae to create biofuels, altering a plant's DNA to make its flowers glow in the dark, or constructing a more powerful influenza virus from scratch (for research purposes or otherwise).

Synthetic biology has the potential to solve, and to create, social problems. It represents a tremendous economic opportunity and a considerable threat to public health and security. Now entering a decisive development phase, synbio technologies are beginning to be both commercialized and democratized. As more products created via synthetic biology are going to market, the tools and materials used to apply the technology are also becoming cheap and accessible enough for startups and hobbyists to get involved. The general public has little understanding of the technology and its implications; it therefore arouses attitudes of both enthusiasm and alarm.² Given that synthetic biology involves creating new forms of life, these attitudes are neither unjustified nor surprising. It is critical that measures be taken to facilitate discussion and accelerate understanding of synthetic biology so that a code of ethics and policies for its use can be developed. The best way to understand the issues and determine policies to regulate the synbio field is to cautiously embrace a culture of open, transparent, and participatory science that promotes discussion of opportunities and consequences at every turn.

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COMMERCIALIZATION (IN YOUR NEIGHBOR'S GARAGE)

While the pharmaceutical industry has used synbio to manufacture products—including synthetic human insulin—for over 30 years, materials produced through synthetic biology are beginning to appear in household products with increasing frequency. Ecover, a Belgian cleaning-product company, currently markets a liquid laundry detergent that contains oil produced by genetically engineered algae.³ Swiss-based Evolva has constructed a synthetic vanilla that is expected to be the first synbio-produced food additive to hit the market.⁴

The science is also entering a stage of commercialization in which companies are marketing “do-it-yourself” synbio products. A growing movement of “garage biologists” or “biohackers” (referred to as “DIY synbio” in this paper) are using digital tools to design DNA sequences, then assembling them using biological materials that can be purchased online. The increased access to these activities by entrepreneurs and citizen scientists outside of universities, big corporations, and government agencies (“big bio”) is the result of dramatically lowered barriers to entry in terms of formal education, bureaucracy, and cost.⁵ The DIY synbio movement fundamentally challenges the way scientific knowledge is structured and controlled, as it essentially enables anyone to access and contribute to biomedical research. Whether DIY synbio ultimately disrupts or complements the work of the existing big bio regimes, including academic institutions, corporations, and government agencies, will depend on whether big bio chooses to embrace it, ignore it, or fight it.

Genomikon, a startup whose tagline is “Genetic Engineering for Everyone,” markets a consumer “wetware” kit that can be purchased online for about \$500.⁶ A wetware kit is a consumer product that provides all the biological materials, instructions, and troubleshooting tips to enable experimentation in the lab or in the home. Synthetic biology is frequently compared to computer programming. A wetware kit is much like a software development kit that enables users to create applications for a particular software platform—the significant difference being that, rather than programming software, the user is programming living matter and manipulating the functions of cells by altering the genetic code.

If programming cells becomes as accessible as programming software, DIY synbio could become a new medium that people use to express themselves, much like computers and the Internet. Moreover, if this synbio “democratization” continues to scale, we could see the creation of entirely new industries.

The mix of scientists, amateur tinkerers, artists, and entrepreneurs who comprise the DIY synbio community embodies an idealist countercultural ethic that is reminiscent of the early computer hackers. In the 1970s and 1980s, the Homebrew Computer Club met regularly to exchange ideas about the future of personal computing. That group included the likes of Apple founder Steve Wozniak. In terms of drive and capability, the DIY synbio community looks very similar, which raises an obvious question: could DIY synbio drive the same kind of economic growth and social change as personal computing? Are we perhaps seeing the dawn of con-

sumer biology? The growing sense of curiosity about synbio among non-scientists speaks volumes about the market potential of democratized life science. Bill Gates once envisioned putting a computer on every desk. Why not a biolab in every home?

For all the similarities between IT and synbio, there is of course one glaring difference. Computer scientists work in silicon and code. Synthetic biologists are playing with living organisms; thus the risks are far more extreme. Although information technologies can be weaponized and difficult to control, biomaterials pose a far greater threat. While potential upsides of synthetic biology are great, altering DNA can produce new species for which humanity needs to be responsible. Because of the complexity of the field and the velocity of progress, policymakers must engage immediately and continuously with the DIY synbio community.

The tools biohackers already use promote sustained openness and transparency; accountability is implied. The DIY synbio community's current activities are self-regulating: they facilitate continuous risk assessment by virtue of the fact that they rely on the open sharing of information. Processes and results are crowd-reviewed rather than peer-reviewed. Thus, they can be tested and verified, and their ethical soundness and safety can be assessed, by a larger group of peers and at a faster rate than traditional closed-lab experiments.

Properly assessing and addressing the issues surrounding DIY synbio requires a view of what it looks like at the ground level. Seeing the movement in action promotes understanding of the economic and educational opportunity the field could provide. It also makes it clear that, although the risks involved in DIY synbio are real and cannot be ignored, they also are manageable and should be carefully addressed rather than fearfully suppressed. The most effective way for regulators to keep tabs on DIY synbio is to become involved. Go to the source and take part in the discussions and activities guiding the future of the discipline. The following section presents a firsthand account of the still unfolding #Sciencehack project and provides a ground-level view of DIY synthetic biology in action.

DIY SYN BIO IN ACTION

One Friday in 2014, a yellow school bus full of biohackers headed from Toronto to Haliburton, Ontario. Armed with DNA segments, pipettors, petri dishes, disposable gloves, and a \$199 incubator, the group checked into the Pinestone Resort for the weekend. There, and in a lunchroom at Fleming College's Haliburton School of the Arts, they would design and construct new life forms.

The group of biohackers, which included some "real scientists" as well as designers, artists, writers, and computer programmers, was specifically trying to create synthetic violacein, a compound that has shown promise as an antibiotic to fight parasites, as well as anti-tumorigenic properties that warrant further research into its potential as a cancer treatment. In nature, violacein is produced by soil-dwelling tropical bacteria as a defense against amoebic predators. A gram of violacein costs around \$300,000.⁷ The loose consortium of doctors and dabblers in

the Haliburton group hoped to reduce the cost dramatically by designing new metabolic pathways that would boost the amount of violacein production in *E. coli*.

The weekend-long hackathon in Haliburton, called #Sciencehack, was organized by Synbiota, a Toronto-based startup that took home the top prize in the Innovative World Technologies category at the SXSW Interactive Accelerator held earlier this year. Synbiota's web-based open-science platform is effectively a lab on a browser that does for scientific research what tools like Google Docs have done for collaborative writing or what mass open online courses, or MOOCs, are doing for education. All experiment results are shared and open for public view. In fact, #Sciencehack was also live-streamed in the name of transparency, thus opening a window to those interested in peering into the DIY synbio realm.

While Synbiota provides the software for virtual science, Edmonton-based Genomikon provides the wetware for material science. Genomikon's "Violacein Factory" kit is equipped with all the necessary biological materials and instructions to create the plasmid violacein. The collaboration between Synbiota and Genomikon opens and democratizes genetic engineering in a way that fundamentally upends how scientific research has been done. They believe that Mass Open Online Science (MOOS, as it was coined at SXSW) or, as Synbiota prefers to call it, Open Distributed Genetic Engineering could greatly increase the rate at which new scientific breakthroughs are made.

The #Sciencehack event in Haliburton was the first of its kind and it marked the beginning of a research sprint led by Synbiota and Genomikon to discover new biodesigns for creating violacein. Since then, researchers around the world have worked with the Factory kit and shared their findings in an attempt to engineer a safe strain of *E. coli* that produces violacein on demand. To date, 79 researchers have designed 54 DNA sequences over the course of six #Sciencehack events, and isolated hundreds of violacein colonies. The most recent #Sciencehack event took place in the home kitchen of MIT media lab director Joi Ito in Cambridge, Ma. Ito was so excited by his first biohacking experience that he subsequently invested in Synbiota and donated to iGEM (a synthetic biology competition for students).⁸

One #Sciencehack participant, Alejandro Saettone, produced approximately \$20,000 worth of violacein with his genetic design. He has since applied for a grant to develop protocols for extracting and purifying the enzyme in order to test its toxicity in cancer cells. Saettone thinks that "any organized company could produce and sell violacein on a 'for research use only' basis⁹." Violacein, of course, could not be legally sold for treatment purposes because the product has not yet been through clinical trials. When you think about what Saettone accomplished, it's only a small leap to imagine a garage scientist creating a more efficient pathway to a blockbuster biopharmaceutical. An enterprising biohacker might even take the next step and organize a company and sell his version of the biologic—or he might simply bootleg it.

Synbiota's CEO Connor Dickie is a 36-year-old entrepreneur who studied at Ray Kurzweil and Peter Diamandis's Singularity University. Dickie considers

#Sciencehack a way of building “a huge corpus of information, an online repository of data that is available to anyone.” Dickie knows it goes against convention, to which he says, “This is different from a traditional lab [that] would do the same type of work that we did, but not necessarily share that work with other labs in parallel.” For Dickie, however, the most exciting part of #Sciencehack has been “finding out that a bunch of people, non-scientists, who are just generally interested, have the balls to travel to the middle of nowhere on a school bus to do science.”¹⁰ What binds the participants in #Sciencehack is not necessarily any shared discipline or vocation, nor even a particular interest in biology: what the participants have in common is a genuine curiosity and the fervor that comes from being a part of something new, uncharted, and not yet legislated.

Pantea Razzaghi, Synbiota’s chief cultural officer, says, “We all have different backgrounds. I am very much focused on bringing these tools and resources to communities outside of the expected biowalls, pushing the future of biology into new areas.”¹¹ The fact that a biotech startup has a chief cultural officer is telling in terms of the company’s larger mission. Synbiota is not just democratizing synthetic biology by making it more accessible, it is socializing it and making it more acceptable to many, including regulators, whose fears could hamper the discipline.

ACCELERATING UNDERSTANDING BEFORE POLICY

The roads being laid by synbio entrepreneurs like Genomikon and Synbiota certainly signal the growing importance of garage biology as a source of innovation across sectors. Put simply, the more people participating in synbio, the faster it may produce breakthroughs that generate wealth, benefit human health, and reduce strain on the environment. But DIY synbio also makes more accessible the tools, materials, and knowledge needed to create and manipulate WMDs, such as avian influenza or *Bacillus anthracis* spores—commonly known as anthrax.¹² More troubling is the spectrum of possible activities that are not so black and white, to say nothing of applications that we cannot at all yet imagine. Gioietta Kuo, a senior fellow at the American Center for International Policy Studies, points to the present moment as a key juncture for bioethics: “Our technical ability has reached a point where we can alter the world for the better or worse. But which is which?”¹³ One can easily imagine utopian and dystopian scenarios for a future highly influenced by biotech; the conditions of that world will depend greatly on decisions made today.

A progressive policy determination model is required. The participatory activities already being practiced by the DIY synbio community provide an optimal venue for dialogue. By its very nature, the DIY synbio community invites stakeholders from various sectors—education, industry, policy, and security, for example—to take part. It is up to these and other communities to participate and communicate directly with those active in the DIY synbio movement, where the discussions are already taking place and bioethics decisions are being made in real time as the technology advances.

A code of ethics has been drafted by the global community, DIYBIO, and posted at DIYbio.org. It emphasizes transparency, knowledge sharing, modesty, accountability, peaceful purposes, and safe practices.¹⁴ Within this framework, further regulations can be established that will promote safety and security without stifling research and innovation.

POLICYMAKERS FEAR WHAT THEY DO NOT UNDERSTAND

As with most technologies from cars to computers, there will always be risks of misuse and dual use, or simply unintended mistakes and unforeseeable outcomes. Synthetic biology is no different in this respect. No matter how many oaths, declarations, safety inspections, tripwires, laws, and policies are developed and enforced, none will dissolve the inherent risk in interactions between nature, technology, and humans. Even in an environment where there is common agreement of intent, there are and will be many uncertainties associated with developing synthetic life. It is indeed possible that an individual or group could take advantage of the DIY synbio community's accessible tools and open-source information and use them for malicious purposes in secret. But this is also why it is so important to maintain open and inclusive dialogue, so that the DIY synbio community, which has thus far proven to be of a high moral and ethical standard, can continue to report openly, serving as watchdogs over their own unconventional labs.

Hindering such conditions are instances where the security community has acted unjustly and hostilely to the synbio community. In 2004, the FBI detained bioartist Steve Kurtz under suspicion of bioterrorism, even though his projects were legal. Such acts by authorities have resulted in fear-based secrecy by some "garage biologists" in a community that otherwise champions transparency. Rob Carlson, a leading expert on synthetic biology, says "a direct result of the DOJ/FBI attitude is that people with labs at home have stopped talking about those labs, which has had the effect of making more DIY scientists want to practice secretly rather than talk about it and engage openly."¹⁵ It is only via constant communication and close collaboration among stakeholders that safe policy and security solutions will be determined and upheld. Fear-based suppression by authorities will only result in fear-based secrecy by the DIY synbio community; such a cycle has the effect of increasing uncertainty and potential threats.

HACKING BIO AND POLICY

The culture of biohackers—their tools, spaces, and techniques—is becoming policy itself. The makeup of the community and its technological and ethical limits are inseparable from a system of rules. Embedded within the tools of open science is the importance of monitoring processes and results. Just as author-activist Jane Jacobs proposed a theory of "eyes on the street" to create the conditions for safe urban living, saying that "a well-used city street is apt to be a safe street,"¹⁶ we see the bio community building affordances—that is, properties of a thing that deter-

mine how it could be used—and support for “eyes on the strand,” where DIY synbio culture, its social protocols, and its tools become a viable methodology for risk assessment. One might say that a trait for self-regulation is encoded into the community’s figurative DNA.

The whole idea of citizen science is centered around crowdsourced data and on building on the breakthroughs of others as they happen: transparency and accountability are inherent. An effective regulatory framework for DIY synbio should be able to absorb any new elements that enter the field in real time. However, sustaining such a responsive model will require constant conversation, collaboration, and cross-pollination among stakeholders in all sectors, which will enable the roadmap to adapt as new elements are introduced onto the landscape.

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