CHAPTER 35

Synthetic Biology


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Framing the Issue

Using a number of technologies and intellectual approaches, synthetic biology solves biological engineering problems by designing and reconstructing new biological parts, or systematically redesigning existing, natural biological systems. Implicit in this process are some as-yet unresolved issues for policymakers. For example, some applications of synthetic biology that benefit society could also be applied in ways that can harm it, or that could be unintentionally dangerous; the use of such technologies in the development of a biological weapon, such as a virus, is an obvious concern. But also of concern is that scientists who are carrying out legitimate experiments could without malice construct an organism with disease-causing potential.

The issue of safety is further complicated because applications of synthetic biology that are considered beneficial by some may be perceived as harmful or dangerous by others. Perhaps the best-studied example of this sort of disagreement is that of the introduction of genetically engineered (often referred to as “genetically modified”) food crops. Use of these crops may bring benefits, such as the possibility of using less pesticide, yet many consider any such modification to be inherently harmful in the absence of compelling evidence to the contrary.

Discussion and debate regarding these issues need to engage practitioners (including students), policymakers, research administrators, and commercial providers of raw materials for the research, both among themselves and in conjunction with a diverse range of interested citizens and civil organizations.

Background and Science

The concept of synthetic biology as an approach to biological engineering dates to the mid-1970s when the advent of readily available enzymes and other materials allowed pieces of DNA to be easily swapped between organisms. The last 10 years have been a time of tremendous improvement in the ease of specific techniques associated with synthetic biology, and this, along with rapidly falling costs and the dispersion of experimental approaches once thought to be the domain of elite biologists, has resulted in the dissemination of synthetic biology widely (among sectors and academic approaches) and deeply (from Nobel Prize winners
to high school students). Recent results of such experiments include:

- The construction of an infectious poliovirus genome from oligonucleotides (short fragments of DNA that are strung together in the laboratory)
- The reconstruction of bacteriophage T7 to simplify its genome (demonstrating that naturally occurring genomes can be systematically redesigned and rebuilt for further research or for specific applications)
- The synthesis of a 582,970-base-pair genome of Mycoplasma genitalium (showing that the full genome of a replicating organism can be constructed in the laboratory)
- Practical applications, including an attempt to produce artemisinin, the precursor to the malarial drug artemisin, that are very close to succeeding.

Although other biotechnologies could in many cases be applied to essentially the same purposes, the combination of easy access to synthesized DNA, powerful computers to aid design, and the distribution of these technologies to users beyond the “traditional biologist” have raised unique safety and security concerns about synthetic biology. Further, the idea of using these technologies to construct living organisms has sparked discussions about whether the use of these technologies is ethical and, beyond that, what “creating life” means. Ensuring that this field develops in a responsible manner, respectful of society’s desires and beliefs, will require some combination of training, oversight, and community external or self-regulation, constructed to allow the science and engineering to advance without compromising safety, security, or society’s values.

**Ethics, Society, and Synthetic Biology**

We discuss here five major areas of concern with respect to the societal impacts of research in and applications of synthetic biology. These include biosafety and biosecurity; the environment; ownership; philosophical and theological issues; and the professional conduct of researchers. Some of these issues have been very well analyzed; for others analysis is just beginning. Each is outlined below.

**Biosafety and biosecurity.** A key set of technologies for synthetic biology is the construction of DNA in the laboratory from its constituent chemicals. Often referred to as “DNA synthesis,” “gene synthesis,” and “synthetic genomics,” this set of technologies makes it possible to build DNA of any specified sequence and length, up to the size of a whole genome. The biosafety and biosecurity implications have been explored by the authors and others in some detail (in “Resources” box, see Garfinkel et al., National Science Advisory Board for Biosecurity, and Tucker and Zilinskas).

For our 2007 study, a working group of experts in the technologies of DNA synthesis, research applications of DNA synthesis, engineering, policy, law, ethics, and sociology conducted a technology assessment of synthetic genomics. Over 20 months, we systematically explored the potential risks and benefits of synthetic genomics; the technologies that currently exist for carrying out the research; and the technologies that may be available in five to ten years. The analyses aimed to identify the benefits and risks that were specific to synthetic genomics as opposed to biotechnology generally.

We found that, with very few exceptions, synthetic genomics would not now be the technology of choice for a bioterrorist or nation-state hoping to develop a virus for use as a weapon. Within five to ten years, however, it may very well be the case that synthesis will be easier than other means of obtaining a virus.

Based on these qualitative analyses, we constructed a list of 17 possible options for governance, focusing on the commercial suppliers of DNA; the machines and reagents that can be used to synthesize DNA in laboratories; and the legitimate users of these technologies, including their associated organizations, such as universities. These options range from requiring that firms screen every order for potential malicious intent to extending the mandate of institutional biosafety committees to consider the potential security implications of experiments.

Commercial firms that make and sell synthetic DNA have in fact already recognized that they have a role in assuring the safety of researchers and communities nearby and the security of all. Several firms have together formed the International Consortium for Polynucleotide Synthetics (ICPS). ICPS members and others have published a potential oversight framework for the development and implementation of sequence screening tools and mechanisms for reporting and resolving concerns about orders of potentially dangerous sequences.
The U.S. government is also examining the risks from synthetic biology, particularly from the biosecurity perspective. The National Science Advisory Board for Biosecurity (NSABB) recently released recommendations for dealing with the synthesis of select agents. Various agencies are participating in the U.S. government review of these recommendations, and the NSABB and others are continuing work on assessing whether the mechanisms of prior review of experiments by local institutional biosafety committees will need to be modified to accommodate security and safety concerns associated with synthetic genomics.

Other countries have noted concerns about this technology, as well. In Europe the concerns are generally more directed toward biosafety, particularly as related to accidental releases of synthesized organisms.

Environment. Synthesized microbes might be intentionally or unintentionally released to the environment. Concerns about the potential environmental impacts of the accidental release of engineered synthetic microorganisms are closely related to concerns about biosafety and the impact of an accidental release on communities immediately surrounding laboratories. The accidental release of a truly novel organism is worrisome, as there would be, by definition, no prior experience with how it would act in a specific environment. However, highly modified microorganisms are unlikely to survive in a natural environment.

With respect to planned releases, synthesized organisms would be subject to the same regulations as any other genetically modified organism. For example, in the United States, the Environmental Protection Agency, Food and Drug Administration, and the Department of Agriculture all regulate the introduction of various foods, drugs, pesticides, herbicides, etc., including those that are genetically modified. The question is whether organisms should be subject to a greater degree of scrutiny simply by virtue of having genomes that had been modified using synthetic DNA, rather than DNA extracted from another organism.

Ownership: access, sharing, intellectual property, and innovation. Synthetic biology may pose special problems for those seeking ownership of, or access to, what might become vast arrays of new technologies. Both patent thickets (the need to receive licenses from multiple patent-holders) and the “anticommons” (many patent owners blocking each other) are potential roadblocks to the use and distribution of these technologies. This is an area that will need significant attention as the field develops. It is being studied by several groups within the academic legal community, such as the Center for the Public Domain at Duke Law School and the Samuelson Clinic at the University of California Berkeley School of Law (see Chapter 20: Intellectual Property and Biomedicine).

Philosophical and theological issues. One application of synthetic genomics is to build a microorganism containing a “minimal genome,” defined as the smallest set of genes that would permit an organism to live and reproduce in a specific environment. The idea is to construct the minimal genome of a particular bacterium, insert that genome into a cell, and show that the resulting organism can replicate. Such a microorganism would help scientists to better understand the basic functioning of cells, or perhaps be a platform for biotechnology applications.

This potential application led to one of the first robust ethics analyses of the field, which was published in 1999 by Cho and colleagues (see box: “Resources”) and preceded any actual work on constructing an organism with a minimal genome. The analysis took into account issues of religion, commercialization, and the potential benefits of the...
research. It also looked at concerns about reductionism—that is, the view that a cell or an organism is only the sum of its parts—in this case, genes. This view is particularly problematic for those individuals—be they scientists, philosophers, or theologians—who think about the interaction of cells or organisms with the surrounding environment.

Construction of a minimal genome thus can raise distinct questions as to whether and how such work can contribute to or change the definition of life, and whether policies are needed to assure an equitable distribution of benefits from such research. At the time, those researchers concluded that constructing a minimal (or even new) genome does not violate any moral principles. Others have disagreed with this assessment, and little additional rigorous analysis has been done in the last nine years.

However, there is a clear need for ethicists, theologians, scientists, engineers, policymakers, and the public to understand each others’ views on these issues, and such examinations are ongoing. The Venter Institute is continuing its efforts in this area. The Hastings Center has recently embarked on such a project, called *Ethical Issues in Synthetic Biology: Toward Clearer Understanding and Better Policy*, funded by the Alfred P. Sloan Foundation.

**Professional conduct of researchers.** Codes of conduct, ethics or practice have been considered for biological science in general, and synthetic biology in particular, but none have yet been adopted. Engineers have long worked under various codes of conduct. Training students on aspects of professional responsibility and ethical conduct is a critical feature of the process leading to adherence to these codes and has long been a part of engineering curricula. Devising standards of practice might eventually be a task for any professional society.

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**RESOURCES**

**Web sites**

- [http://polysynth.info](http://polysynth.info) – The International Consortium for Polynucleotide Synthesis. Includes links to participating international synthetic biology companies and some resources.
- [http://synbiosafe.eu](http://synbiosafe.eu) – Synbiosafe. This European Union–funded project aims to proactively stimulate a debate on issues in synthetic biology; includes project products and an online discussion forum.
- [http://www.syntheticbiology3.ethz.ch](http://www.syntheticbiology3.ethz.ch) – Synthetic Biology 3.0. The conference site for the Third International Meeting on Synthetic Biology, held in Zurich in 2007, includes videos of the talks and proceedings available for download.

**Recent news**


**Further reading**

developed for synthetic biology (see Endy in “Resources” box). But whether or not synthetic biology as a discipline articulates a full code of conduct, such codes have been and likely will continue to be communicated to students and researchers in the field at forums such as the International Genetically Engineered Machine Competition, where the participants are mainly undergraduates from various disciplines and national origins, and the series of annual international synthetic biology meetings, where a wide variety of students and researchers gather.

In 1971, in describing the content of a talk in a conference he was organizing, Sidney Fox wrote, “As such processes [of synthetic biology] are brought under control in the laboratory, they have increasing implications for society and its philosophy.” This is perhaps even truer today, as the full implications of the science and engineering are only now being appreciated.

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2. Similar to synthetic biology, biological engineering exploits new developments other biological fields however biological engineering applies these breakthroughs to understand living systems with the goal of solving natural problems with these systems.

3. Systems biology is focuses on the study on natural systems, often with some long term medical significance. But the work is fundamentally an engineering application of biological science, rather than an attempt to do more science.

4. The Controversy.


7. Unpalatable truths about laboratory-grown food. A meeting on synthesising the human genome, convened behind closed doors at Harvard, has caused a stir. Synthetic biology is an interdisciplinary field, best defined as engineered solutions inspired by biology to create renewable, biodegradable, and safe materials. Synthetic biology has found applications in several areas, including healthcare, agriculture, and biomanufacturing of textiles, ink, and other consumer products. Advancements in precise genome engineering tools such as CRISPR have further boosted the scope of this field.