Bioindustrial Ecology

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In the early 1990s, one of the foundational articles on industrial ecology raised an interesting question: "Is there a good industrial analogue to the microorganism?" (Frosch 1992, 801). At that point in time we were used to thinking of microorganisms as different from industrial processes. Recombinant DNA, genetic engineering, and now synthetic biology have blurred that distinction. The Polish geneticist Waclaw Szybalski used the term *synthetic biology* in 1974 to describe a field with "unlimited expansion potential and hardly any limitations to building 'new better control circuits' [and] finally other 'synthetic organisms'" (Szybalski 1974, 405).

If industrial ecology is built on the premise that we can engineer industrial systems to mimic nature, synthetic biology strives to engineer nature to change industrial systems through the design and construction of new biological parts, devices, and systems and the redesign of existing ones.

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Until recently, engineering biology was slow, haphazard, and expensive. It often took years and hundreds of millions of dollars of research and development (R&D) to create new biologically engineered materials and products. Synthetic biology promises to make biology easier and faster to engineer. Many of the capabilities that enabled the last industrial revolution are finding their way into biology: the standardization of parts, interchangeability, and modularization. These changes will support reproducible precision processes built on the ability for rapid prototyping, compressed design-build-test cycles, and controlled variability—the hallmarks of mature industrial production systems. The costs driving these changes are dropping exponentially. In 2007, sequencing one million DNA base pairs cost around $10,000—it is now 10 cents, and the cost of sequencing an entire human genome is approaching $1,000.

The parts catalogue is expanding. For example, an online, open-source registry of biological parts[1] now contains more than 16,000 components with a broad range of functions, from biosynthesis to odor production and sensing. This is creating a plug-and-play infrastructure for biological experimentation. Using these parts as a starting point, hundreds of students a year now compete in an international competition to create genetically engineered machines (iGEM).[2] As genetic sequencing becomes exponentially cheaper, the code could be downloaded and the parts produced locally, enabling distributed innovation and production systems.

How big could the impacts of synthetic biology be? Recent market projections by Transparency Market Research (Albany, NY, USA) indicate that the global market for synthetic biology is likely to grow to $16.7 billion by 2018,[3] with chemicals and energy constituting the largest share. A preliminary inventory recently compiled by the Synthetic Biology Project at the Woodrow Wilson Center (Washington, DC, USA) found a wide range of applications moving toward commercialization, including adipic acid (nylon precursor); succinic acid; modified polybutylene; lactic acid; food additives; biodispersants; bio-acrylics; a range of biofuels; drugs to treat diabetes, cholera, cancer, and hypertension; and applications to prevent insect-borne disease (using engineered gene circuits that can spread through wild populations to prevent the transmission of malaria).[4]

Synthetic biologists are already utilizing a wide range of organisms ranging from blue-green algae (cyanobacteria) to yeast and *Escherichia coli*. California Institute of Technology (Pasadena, CA, USA) researchers successfully modified baker's yeast (*Saccharomyces cerevisiae*), using genes from plant enzymes, to produce benzylisoquinoline alkaloid (BIA) molecules, which can form the basis of a wide variety of drugs with antispasmodic and pain relief effects, including morphine. Metabolic pathways in yeast have also been engineered to produce artimisinen, the prime ingredient for antimalarial drugs. Researchers at Harvard University (Cambridge, MA, USA) have transformed cyanobacteria into a highly efficient sucrose factory, achieving yields five to six times those from sugarcane.

The future is much more radical. A multimillion dollar synthetic biology program at the Defense Advanced Research Projects Agency (DARPA), called *living foundries*, seeks to transform "biology into an engineering practice [which] would

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enable on-demand production of new and high-value materials, devices and capabilities."[5] In May 2010, the U.S.-based J. Craig Venter Institute (Rockville, MD, and San Diego, CA, USA) created the first self-replicating cell with a synthetic genome (the parent was a computer). Fully synthetic life is not far away and with it comes the possibilities (and dangers) of more radical alterations of life and bottom-up engineering of a wide range of bio-based functionality that could not be achieved through traditional genetic engineering approaches. Except for the National Aeronautic and Space Agency's (NASA) Office of Planetary Protection in the United States, set up to consider the transfer of novel biological matter between planets, few organizations have thought through the implications of truly synthetic life forms.

Even at this stage of its development, synthetic biology has many of the key characteristics of so-called general purpose technologies (GPTs): a pervasive impact across multiple economic sectors and products, the ability to spawn innovations across value chains (for instance, in intermediary and downstream sectors/products), and significant potential to improve cost and productivity. In the past, GPTs such as electricity, steam power, and chemical synthesis have replaced established technologies, often in a disruptive fashion.

One disruptive shift would be moving from a hydrocarbon to a renewable carbohydrate economy. Engineered microorganisms offer distinct advantages over existing crop-based approaches to biomass production (like cellulosic ethanol), including inexpensive inputs (sunlight, carbon dioxide [CO_2], and some nutrients), high photosynthetic conversion efficiencies (3%–9% for some cyanobacteria, for instance, versus less than 0.25%–0.3% for terrestrial plants), very rapid growth rates, and adaptability to nonarable land with no competition for food production (Ducat et al. 2011). In the area of biofuels, high production efficiencies could result in order-of-magnitude reductions in the amount of land required for production. In addition, synthetically engineered organisms can produce "drop-in" fuels that utilize the existing distribution infrastructure and do not require blending or further modifications.

Many organisms can be engineered to provide multipurpose feedstocks supporting industrial symbiosis. For instance, sucrose produced by engineered cyanobacteria could be used as an input to produce ethanol, biodiesel, butanol, solvents, antifreeze, sorbitol, glycerol, polyamides, and bioplastics. This would allow the creation of "microbial industrial parks" supporting the colocation of different high-value production systems with reduced transport costs. Microbial production systems could potentially use the outputs of other processes, such as captured CO_2 from power plants. Synthetic microalgaes used to produce biodiesel could result in a variety of high-value by-products, including nutrient-rich fertilizers, high-protein animal feed, and biogas (Chisti 2008).

Significant challenges remain, however, especially in terms of scaling lab-based processes and proactively addressing any emerging social, ethical, and environmental issues arising as the field grows. Synthetic biology has already triggered two major studies on its potential ethical implications, the first by the European Group on Ethics in 2008[6] and the second, in late 2010, by the President's Commission for the Study of Bioethical Issues.[7] Security experts worry about the potential to create a new generation of bioweapons. A global coalition of nongovernmental organizations lead by Friends of the Earth issued a report in 2010[8] calling for "a moratorium on the release and commercial use of synthetic organisms and their products to prevent direct or indirect harm to people and the environment."

The introduction of synthetically engineered organisms into the environment will require parallel work to assess and manage any concomitant risks, especially as these organisms depart further from natural referents. Ecologists, as well as many evolutionary and environmental biologists, view this field with some trepidation and have raised valid questions concerning the stability of synthetic DNA, its persistence in the environment, the fate and transport of synthetic organisms (biological material can move through aerosolization, wildfowl vectors, extreme weather, and human error), horizontal gene transfer, and a lack of adequate funding to assess risks (using scenarios and micro- and mesocosms, for instance) (Dana et al. 2012)

A transition to bioindustrial systems based on synthetic biology will provide some new challenges and opportunities for the field of industrial ecology. It also may represent the next stage of evolution, one that enables more sustainable production systems based less on biological analogy and more on a new capacity for biological design and engineering. Why mimic biology when we can engineer it?

Notes

1. www.partsregistry.org.
2. http://igem.org.
3. http://www.prnewswire.com/news-releases/synthetic-biology- market-is-expected-to-reach-usd-167-billion-globally-in-2018- transparency-market-research-166861956.html
4. Inventory available at www.synbioproject.org/library/inventories/applications_inventory/.
5. www.darpa.mil/Our_Work/MTO/Programs/Living_Foundries.aspx.
6. See http://ec.europa.eu/bepa/european-group-ethics/index_en.htm.
7. See http://bioethics.gov/cms/synthetic-biology-report.
8. See www.foe.org/news/archives/2010-09-report-synthetic-biofuels-not- a-solution-to-the-clim.

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