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Life from Scratch

Promise, Peril, and Pathogens: Breakthroughs in Synthetic Biology

In November 2003, J. Craig Venter, the famed trailblazer of the genomics frontier, and Spencer Abraham, the Secretary of Energy, convened a press conference to announce a breakthrough in modern biological technique: Researchers working at Venter's Institute for Biological Energy Alternatives (IBEA) had synthesized a complete and fully functioning virus from DNA building blocks, creating artificial life far faster than any previous laboratory.

Soon, the two predicted, this research would lead to the creation of significantly more complex forms of artificial life—and possibly the synthesis of entirely new classes of organisms. As Secretary Abraham explained, IBEA's research, which is funded handsomely by a Department of Energy initiative called "Genomes to Life," takes a substantial step toward creating specially-designed artificial microbes that have the "biological abilities to produce hydrogen, accelerate environmental clean-up, and mitigate the long-term impacts of climate change through sequestering carbon dioxide."

The nascent field of synthetic biology seems to promise a world transformed by "living technologies"—designer microbes that can perform useful tasks, like gobbling up pollution or manufacturing desirable chemicals. But building living organisms from scratch is a tricky business. Scientists can synthesize small strands of DNA with relative ease, but these threads need to be pieced together to create the full genetic sequence of a viable genome. In 2002, researchers at the State University of New York (SUNY) at Stony Brook announced they had synthesized a copy of the polio virus by stringing DNA strands together. But using their method, it took three years to complete the virus, and even then it was a genetic dud—not nearly as robust or virulent as the naturally-occurring polio virus.

Venter, however, has a reputation for pulling off impressive biotechnological feats faster than others—and IBEA's virus was no exception. Using a new technique, the IBEA team was able to persuade the constituent DNA strands of a bacteriophage virus practically to assemble themselves. Unlike the SUNY polio virus, the IBEA bacteriophage was highly infectious. The effort took just two weeks.

Secretary Abraham pledged a full scientific review of IBEA's work and announced the creation of a special committee in the Department of Energy to identify the full range of synthetic biology's future applications.

Despite this excitement in official circles, public reaction to these recent advances has been remarkably mute—especially by comparison to past brouhahas set off by advances in genetic engineering. In the 1970s, for instance, public concerns over man "playing God" with life, and over whether scientists would ultimately be able to control their creations, led the scientific community to impose a short-lived moratorium on research using recombinant DNA (rDNA) technology. In time, those fears dissipated, and today rDNA has a vast array of applications. So far, rDNA technology does not seem to be dangerous.

No one knows whether the same will be true of synthetic biology, but researchers today are proceeding with little concern. Venter and Abraham were eager not to dwell on the potential hazards of the research. As Venter said, "I think the positive applications of this so outstrip the hypothetical negative ones that this will become a widely used technology."

But consider those hypothetical negatives: In November 2003, the Central Intelligence Agency released an unclassified report, "The Darker Bioweapons Future," which claimed that synthetic biology could make possible new highly virulent, drug-resistant, unconventional pathogens "worse than any disease known to man." Moreover, the report asserted, recent advances in biological science and technology were so "broad, complex, and widely available to the public" that traditional means of monitoring the development of weapons of mass destruction could "prove inadequate to deal with the threat from these advanced biological weapons."

Case in point: The SUNY researchers involved in the creation of the artificial polio virus obtained all of the DNA threads for their project from private companies through the mail, and they used a map of the polio genome available on the Internet. The genetic blueprints of a host of other dangerous pathogens—including Ebola, influenza, smallpox, and anthrax—can also be found online. The SUNY scientists warned that current biosecurity regulations, which focus almost exclusively on restricting the proliferation of extant pathogens, are not sufficient to guard our nation against the new generation of biological threats.

With an eye toward these realities, IBEA and Department of Energy scientists conferred with officials from the White House and the Department of Homeland Security before publishing the specifics of their assembly technique. Their work was eventually cleared for publication, because, as the *Boston Globe* reported, "Most scientists consulted by the government believed that terrorists would be unlikely to use such a complex method to stage a biological attack when far simpler ones are available." But other experts disagree. "I could give this to undergraduates, and they could do it," said M.I.T. biology professor Peter Sorger. Indeed, the trend in biotechnology

toward ever-wider distributions of skills and materials makes it likely that the specialized knowledge and resources presently needed for work in synthetic biology will soon be available to those with rudimentary training and few credentials.

The precedent of rDNA technology may mislead us into thinking that everything will turn out alright, and that our worst fears will never come to pass. But rDNA never got out of control because the perceived dangers simply turned out not to be true. If synthetic biology is different—if we are not so lucky this time—the consequences could be grave. We might haphazardly create new tools for our own destruction—easy to build and widely available to those who do not share our commercial, knowledge-seeking, highly civilized ambitions.