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Biologists Are Looking To the Chip Industry For Production Models

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THE CAR ONLY became popular in America after Henry Ford figured out how to mass produce it. Computers didn't invade every office and den until the chip industry learned how to churn out endless billions of the semiconductors that do all of a PC's actual work.

Now, the world's life-science researchers are taking a page from those two industrial playbooks and are trying to make biological production as efficient as most other sorts in modern economies. The economic impact of their efforts could be as significant as what occurred with cars and computers, and could include vastly less expensive gene-based drugs and vaccines, fuel sources and industrial materials.

While individual researchers for nearly a decade have been doing work in this field -- called synthetic biology -- their efforts got a boost last week with the announcement of a \$16 million grant from the National Science Foundation for the Synthetic Biology Engineering Research Center. It will be located at the University of California, Berkeley, and will also include participation from UC San Francisco -- which in the 1970s did much of the pioneering work in recombinant DNA -- along with MIT, Harvard, Prairie View A&M University in Texas and the California Institute for Quantitative Biomedical Research.

Jay Keasling, a professor in Berkeley's chemical-engineering department and director of the new center, says that when semiconductors were first developed in the 1950s, each chip was, in effect, hand-made in an artisan-like process. Chip companies, of course, eventually learned techniques for mass production.

BUT BIOLOGY TODAY is where chips were 50 years ago, he says. A researcher who discovers, say, a potentially useful DNA fragment has no reliable way of mass producing it. Instead, to create large quantities, she must rely on a collection of laborious, hit-and-miss processes, which is the best the field has to offer.

Prof. Keasling says he envisions a day when a biologist can concentrate on difficult science questions and leave production and engineering matters to others. That's the way many chip companies work, creating the designs for their chips themselves, but then shipping off the patterns to "fabs" to get the products made.

Drew Endy, an MIT professor in structural engineering who is involved in the effort, says researchers like himself have learned from the computer industry the importance of three main ideas: standardization, decoupling and abstraction.

The first refers to the way parts in a computer, like the connections to the outside world, are developed to well-known standards. In biology, similar specifications might be developed around the *E. coli* bacteria, a workhorse in producing DNA-based products.

Decoupling refers to splitting a task into multiple parts, the way the computer industry has different suppliers for disk drives, memory and CPUs. Currently, says Prof. Endy, most biology labs do everything themselves.

Abstraction takes a cue from what has happened in programming languages over the decades; software has advanced to the point where programmers increasingly are able to use English-like statements in their code, as opposed to the 1s and 0s of the early days of computing. Prof. Endy says he hopes that future biologists won't need to work on the sort of molecule-by-molecule basis that is used today.

He concedes that the work of synthetic biology may not have the same headline appeal associated with discoveries of new genes tied to specific diseases. But the more prosaic process questions he and the others are tackling are just as important.

WHERE MIGHT ALL this lead? One example, says Prof. Keasling, involves the malaria cure his lab works on, which costs roughly \$2.50 a dose. That's a trivial sum in the industrial West, but it's 10 or 20 times higher than what is affordable in many places where malaria is epidemic. Synthetic-biology tools, he says, could cut prices.

Indeed, the potential for the approach in developing countries is one reason Bill Gates, in his role as philanthropist, has been one of the main private funders of these efforts.

Many researchers are also associated with private companies that hope to profit from synthetic biology. Prof. Keasling promises it isn't the intention to lock up the research behind a fortress of patents.

Instead, he says, the goal is to create an economic and manufacturing infrastructure similar to the one that exists with computer chips. In that world, companies like Intel and AMD are able to make significant profits on their proprietary chip designs. But at the same time, basic design and manufacturing methods are freely available for everyone to use.

His own company might make a low-profit or no-profit malaria treatment, while using similar basic technology to manufacture, for example, biology-based products for the fragrance industry, which would command high margins.

All in all, scientists have made all the headlines in biology research over the past few decades. Now the engineers are moving in, and the real fun can begin.