

The New Biofactories

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Humans have been modifying biological systems for our own economic benefit for millennia. Improvements in crop yields and overall farming productivity have come from a continuing alteration of the genetic makeup—through selection and breeding—of the plants and animals upon which we rely. Now we find ourselves at the dawn of a new age of direct genetic modification. While the term “artificial life form” conjures up images of cyborgs or other creations of science fiction, the first such “artificial” creatures will actually be single-celled microorganisms. Even though these human-engineered life forms will be extremely simple, they will have an enormous impact on our world. Their biggest potential: the creation of biofuels and biomaterials, which have the promise to transform our entire economy.

The first explicitly artificial organisms emerged from recombinant DNA technology in the mid-1970s; this technology was commercialized with lightning speed. As of 2006, biotech drugs accounted for about \$65 billion in sales worldwide. Just one drug, Epogen, has generated \$10 billion in revenues since its creation. A molecular biologist—particularly when receiving stock options in a biotech start-up—would have to conclude that life forms that become “artificial” simply by the addition of one gene can be quite commercially significant.

Revenues from genetically modified “stuff” now exceed 1 percent of US GDP and are generated in three areas: drugs, agriculture, and industrial products like enzymes and plastics. These areas are growing at 10 to 20 percent per year, and together they are making a sizeable and growing contribution to the economy.

The biotech sector is also extremely productive. Between 2000 and 2007, biotech revenues added more than \$100 billion to the economy, representing 2.5 percent of US GDP growth. This was accomplished by a biotech workforce of only about 250,000 people, less than one-sixth of one percent of the national workforce.

Yet the underlying technology is immature compared with that in other sectors of the economy. The majority of biotech products that have reached the market are the result of just a handful of genetic modifications and insertions. The commercial significance of the biotech sector will grow as its ability to engineer new biological systems expands.

Until recently, the complexity of these systems was limited in large part by the cost of development. The labor required to build and test a complex genetic circuit was

prohibitive. But since the mid-1990s, productivity in reading and writing genes has been improving exponentially, while costs have plunged. Now relatively large pieces of DNA can be designed electronically, sent to a gene “foundry,” constructed, and returned via express mail in just a few weeks. It is already technically possible to build stretches of DNA as long as those of small bacterial genomes (about 400 genes).

However, this is not the fastest road to commercially significant organisms. This is because the simpler the engineering task is, the greater the near-term economic impact will be. For example, aeronautical engineers do not attempt to build new aircraft with the complexity of a hawk, a hummingbird, or even a moth. They instead succeed by reducing complexity. Even the simplest cell contains far more bells and whistles than we can presently understand. Consequently, no biological engineer will succeed in building a system from scratch until most of that complexity is whittled away, leaving only the bare essentials. Real progress will come by adding to existing organisms just a few new genes—probably no more than 15.

Companies are already making substantive progress. Amyris Biotechnologies has modified yeast to transform sugar into useful compounds, including malaria drugs and biofuels that can substitute for today’s jet fuel, diesel, and gasoline. The company will begin production of these fuels next year in converted ethanol fermentation plants in Brazil.

As biotech technology develops, biofuels and bioplastics produced this way will be easier and cheaper to make than ethanol or traditional plastics and they will perform better than even petroleum-based products. Their manufacture and use will also reduce the carbon emissions that cause climate change.

Such artificial life forms will fundamentally change how we power the economy, bringing about a switch from fossil fuels to biological feedstocks like sugar, starch, and cellulose. Biomanufacturing is less likely to be centralized, like petroleum refineries and ethanol plants, and will instead be more evenly distributed, like beer breweries.

Cars themselves might actually become the producers of the very fuels they consume. In the spring of 2007, researchers reported the successful construction of a synthetic pathway consisting of 13 enzymes from different organisms that can turn starch into hydrogen. This suggests a future in which sugar or starch—substances available at any grocery store—will go into our fuel tanks instead of gasoline. A fuel cell will use the hydrogen produced by engineered microbes in the tank to provide electric power for the car. Such a car would then become something of a cyborg, relying on living organisms to provide power to an inorganic shell. As one oil executive observed at a recent oil industry meeting, in this model “the car is the refinery”.

If this innovation comes to pass, a very different marketplace is likely to arise. The infrastructure for shipping and refining petroleum overseen by that self-same executive might become less relevant in a new biotech world. Moreover, if distributed biological processing of simple feedstocks can compete in low-margin markets like liquid transportation fuels, then it will also make significant inroads with higher-margin products like fibers, plastics, flavorings, and scents.

It will soon be possible to devise enzymes and organisms that “eat” a diverse array of feedstocks. One good example is municipal sewage. Now mostly treated and disposed of as waste, this resource will initially be used to grow unmodified algae. The algae will in turn be fed to synthetic systems—think of these as “artificial cows”, a fusion of robot and biology that is beyond even the “cyborg” car—engineered to make materials and fuels. Eventually, the algae itself will be engineered to directly convert sewage into products. And inevitably, these artificial cows will move out into the fields, closer to large-volume agriculture. Modern harvesting equipment is already often driven by autonomous, satellite-guided control systems. Imagine robotic harvesters equipped with bioprocessing modules slowly wandering around farmland, consuming a variety of feedstocks, processing that material into higher-value products like fuels and plastics, and delivering it to distribution centers. These hybrid “cowborgs” would thereby become autonomous, distributed biomanufacturing platforms, engineered to supply us with the fuels and materials that we need.

Very few organisms on our planet are larger than about one meter across. Most of the biomass production, and therefore most of the biological processing, occurs at scales of microns to centimeters. While organisms produced by nature face different constraints than those designed by humans, we may find ever more inspiration in microbes, insects, and cows for our future production infrastructure. We have barely begun to tap the promise of biotech.

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