

## The remarkable promise of cell-free biology

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LIVING creatures are jolly useful. Farmers rear animals and then harvest their flesh, eggs and milk for humans to eat. Drug companies genetically engineer animal cells and grow them in vats, so they can churn out drugs to treat disease. There is a catch, however. It is hard work to corral cells and higher organisms to do humans' bidding.

There may be a better way. Cell-free biology, an idea first proposed about a century ago, is at last having its coming-out party. The technique involves extracting the protein-making machinery from living cells. Cell walls, useless molecules and the organism's own DNA are all thrown away. By adding doses of new DNA to the resultant gloop, proteins can then be made to order (see [article](#)). This month, in California, a 1,000-litre vat of cellular machinery belonging to a company called Sutro Biopharma will start churning out components of a cancer drug, which will go through tests with the Food and Drug Administration, America's medical regulator, next year. It will be the first commercial product made in this way. Other firms are working on similar techniques to produce everything from plastics to pesticides. Cell-free biology could also help those trying to produce artificial meat without relying on animals.

It is still early days, and the commercial viability of these techniques has yet to be proved. Synthetic biology smacks to many of "playing God": regulators will have a big say in how quickly the technology is adopted. But divorcing biological production from living things makes sense, for three reasons.

The first is efficiency. Living organisms are shaped by evolution to survive and reproduce. That wastes energy. Consider insulin, which used to be harvested from pig carcasses, and these days is made in vats of genetically modified yeast or bacteria. Those bacteria (and their porcine predecessors) use valuable nutrients to build a host of other proteins besides insulin which are vital for their own survival but worthless to humans. With cell-free biology, more of those nutrients could be turned into the end-product that is being produced.

Living creatures are also irritatingly fragile. Genetically engineered bacteria can be used, for instance, to make a fuel called isobutanol. But it is a solvent, and kills the bacteria before they can make very much. A cell-free system is more robust. Or consider Genzyme, the maker of Cerezyme and Fabrazyme, drugs for treating rare genetic disorders, which are produced in vats of hamster-ovary cells. In 2009 production was stopped for more than a month after these delicate cells caught a viral disease. That shutdown cost hundreds of millions of dollars. But because cell-free production systems are not alive, they cannot fall ill.

The second benefit of cell-free biology is that it has the potential to avoid some of the social and environmental drawbacks associated with relying on living organisms. Growing corn (maize) as a feedstock to make ethanol occupies land that could otherwise be used for growing food, for example. Livestock farming takes up about a quarter of the planet's ice-free land and contributes to climate change. Generating fuel or food in vats could be an attractive alternative.

## A cultural shift

The third reason is ethical. Animals have a capacity for suffering that the cellular machinery from which they are built does not. Modern technology has replaced many natural products with synthetic alternatives. But humans still rely on animals for food, fabrics and a few medicines. Snake farms, crude and expensive, produce antivenom. Factory farming of pigs, chickens and cows has many opponents. Animals' skins and coats, used to make leather and fur, are often the most valuable part of their farmed carcasses. You do not have to be a vegetarian or an animal-rights activist to welcome the possibility of making such products in more humane ways.

There are many pitfalls on the road from the laboratory to mass production. But cell-free biology should be cheered on. Humans will always need the bounty that nature provides, whether in the form of nutrients, drugs or chemicals. But they may not always need living things to produce them.