

Week 6: Biopolymers

Answers to questions due 10/25/06

This is the first half of an article about novel industrial applications of bacterial biochemistry which will unquestionably become highly significant in the coming decade. Note that this article was written in 2003, when crude oil cost about \$25 a barrel (it currently costs about \$60/barrel).

This week: Plastics. Next week: Fuels

Reinventing yesterday

The Economist, Mar 27th 2003

Biotech's biggest use may be to rebuild basic industries

ONCE upon a time, much of the man-made world consisted of things that had been grown. Clothes, carpets, bed-sheets and blankets were woven from wool, flax, cotton or (if you were lucky) silk. Shoes were made of leather. Furniture and fittings were made of wood, which also served as fuel for heating and cooking. Then humanity discovered coal, oil and chemistry. Today only the poorest and the richest people burn wood, and many of its other uses have been taken over by plastics. Natural fibres, too, have ceded much of the market to artificial ones. But biology may be about to revenge itself on the synthetic, petroleum-based industrial world by providing new materials and fuels. And in this guise, it may even become acceptable to the environmental movement.

In truth, biotechnology has been quietly working away at industrial applications for some years. It started with enzymes. A business in purifying and selling bacterial enzymes for use in food manufacturing, washing powders and so on has existed for decades, but in 1988 a Danish firm called Novozymes produced the first transgenic enzyme, a fat-digester for detergents. Partly thanks to this lead, Novozymes is now the world's largest enzyme manufacturer, hotly pursued by several other firms.

Enzymes are proteins, which have a reputation for being fussy molecules. Expose them to the wrong temperature, acidity, salinity or pressure and they stop working, sometimes permanently. And the temperature, acidity, salinity and pressure of industrial chemistry is often very different from that found in familiar living organisms. However, it has become clear that lots of bacteria thrive in conditions that used to be regarded as hostile to life. Quite a cottage industry, known as bioprospecting, has developed to collect these bacteria from hot springs, soda lakes, arctic rocks, industrial-effluent outlets and so on. Enzyme companies then analyse the bugs for proteins that look like useful starting points for the sort of directed evolution used by firms such as Applied Molecular Evolution, Genencor and Maxygen in their search for drugs.

Enzyme-catalysed processes have always been a more efficient way of making molecules than traditional chemistry. They often involve fewer synthetic steps, and the yield of each of those steps is almost always close to 100%, whereas the cumulative losses from step to step of doing things in a complicated traditional synthesis mean that the yield may easily end up below 10%. But until recently, the range of reactions for which enzymes could be used was limited, and their fussiness confined them to high-value products such as drugs and vitamins. Now, thanks to directed evolution, there is serious talk of using enzymes to make cheap, bulk chemicals. And not only talk: action, too.

Material progress

The most promising applications for the new model enzymes over the next decade are plastics and fuels. The two most advanced **plastics** projects are those of DuPont, one of the world's biggest chemical companies, and Cargill-Dow, a joint venture between the agricultural and chemical firms of those names. DuPont's process, developed in collaboration with Genencor, **took biochemical**

pathways from three different micro-organisms and assembled them into a single bacterium.

The raw material for the process is glucose syrup **made from corn starch**. This is converted into a molecule called 1,3 propanediol, which is used to make a polyester called Sorona. But Sorona is only half biological. It is a copolymer—that is, it is made out of two sorts of monomer—and the other one, a molecule called terephthalate, still has to be made from oil, so there is some way to go.

Cargill-Dow is closer. Its product, Ingeo, **is made out of lactic acid**, which in turn is made from glucose. Traditional techniques are used only for the polymerisation of the individual lactic-acid monomers into polylactic acid (the chemical name for Ingeo). The stuff is being made in commercial quantities at a plant in Nebraska, and is about to go on the market. At the moment it is rather more expensive than its petrochemical competitors, but Cargill-Dow hopes to brand it as a premium product in the market for environmentally friendly goods.

Biopolymers are environmentally friendly twice over. Since their manufacture uses little in the way of fossil hydrocarbons, they do not add to global warming. And because they are biodegradable, they cause no pollution when discarded. The firms' bigwigs seem hopeful that this will prove a big enough attraction to allow them to reap economies of scale that will then make their products truly cost-competitive.

DuPont and Dow are giants, but biopolymers can be for minnows too. Metabolix, a small firm based in Cambridge, Massachusetts, takes the process for making them to its logical conclusion—by getting living organisms to do the polymerisation as well as making the monomers.

Animals and plants store surplus energy in the form of carbohydrates, oils and fats. Some bacteria, though, use a different molecule, called a polyhydroxyalkanoate, or PHA. About a decade ago, when they were working at the nearby Whitehead Institute, James Barber and Oliver Peoples, the founders of Metabolix, realised that this material might be put to use as a plastic. They have spent the past ten years proving the point.

Having prospected the bacterial world for appropriate enzymes, and assembled enzymatic pathways in the same way that Genencor did for DuPont, they came up with something new: bugs that actually make plastics and store them inside themselves, in large quantities (about 80% of the weight of a grown bacterium is plastic) and in great variety. PHAs are not a single chemical, but a vast molecular family. Different enzyme pathways can turn out different monomers, producing plastics with different properties. Indeed, it is possible to have two different enzyme pathways within the same bacterium. The result is a co-polymer that expands the range of properties still further.

Metabolix, which plans to start commercial production later this year, has shown that its PHAs, too, can be produced at a price which is competitive with at least the more expensive existing polymers, such as polyesters. That in itself may not be enough to convince manufacturers to switch from tried and trusted materials to Metabolix's novel ones, but the firm hopes that in the large market for single-use items the added feature of biodegradability will be a clincher. If manufacturers do not make the change unprompted, then a nudge from the regulators might be expected. Currently, plastic is a persistent form of rubbish, whereas an object made of PHA will disappear in a few weeks if dumped in a landfill, or even in the sea.

Get the price right, then, and the opportunities are enormous. According to a report published in 2001 by McKinsey, a consultancy, by 2010 biotechnology will be a competitive way of producing about a fifth of the world's chemical output by value. That means white biotech will be competing in a market worth \$280 billion, of which McKinsey thinks the technology might capture about \$160 billion. As biotech processes become cheaper, those numbers will increase.

All the companies working in this field have projects designed to bring down the costs. Metabolix, for example, hopes to switch from growing plastics in bacteria (which have to be fed) to growing them in plants (which will make them out of water, carbon dioxide and sunlight). The firm's researchers have already shown that this is possible in the laboratory. They are now scaling up the process.

Questions.

1. What does the price of crude oil have to do with the use of enzymes to make plastic (biopolymers)? Specifically, tell me whether an increase in the price of fossil fuels will **encourage** or **discourage** the industrial development of biopolymers.
2. Name one raw material/starting material for making a plastic mentioned in this article.
3. Which is more efficient (gives you more product): synthesis of a chemical using enzymes, or using traditional chemistry?
4. If you dump a biopolymer and a traditional plastic in a landfill, which one will still be there in 20 years?