White biotechnology

The application of biotechnology to industrial production holds many promises for sustainable development, but many products still have to pass the test of economic viability

For tens of thousands of years, humans relied on nature to provide them with all the things they needed to make themselves more comfortable. They wove clothes and fabrics from wool, cotton or silk, and dyed them with colours derived from plants and animals. Trees provided the material to build houses, furniture and fittings. But this all changed during the first half of the twentieth century, when organic chemistry developed methods to create many of these products from oil. Oil-derived synthetic polymers, coloured with artificial dyes, soon replaced natural fibres in clothes and fabrics. Plastics rapidly replaced wood and metals in many consumer items, buildings and furniture. However, biology may be about to take revenge on these synthetic, petroleum-based consumer goods. Stricter environmental regulations and the growing mass of non-degradable synthetics in landfills have made biodegradable products appealing again. Growing concerns about the dependence on imported oil, particularly in the USA, and the awareness that the world's oil supplies are not limitless are additional factors prompting the chemical and biotechnology industries to explore nature's richness in search of methods to replace petroleum-based synthetics.

An entire branch of biotechnology, known as 'white biotechnology', is devoted to this. It uses living cells—from yeast, moulds, bacteria and plants—and enzymes to synthesize products that are easily degradable, require less energy and create less waste during their production. This is not a recent development: in fact, biotechnology has been contributing to industrial processes for some time. For decades, bacterial enzymes have been used widely in food manufacturing and as active ingredients in washing powders to reduce the amount of artificial surfactants. Transgenic *Escherichia coli* are used to produce human insulin in large-scale fermentation tanks. And the first rationally designed enzyme, used in detergents to break down fat, was introduced as early as 1988. The benefits of exploiting natural processes and products are manifold: they do not rely on fossil resources, are more energy efficient and their substrates and waste are biologically degradable, which all helps to decrease their environmental impact. Using alternative substrates and energy sources, white biotechnology is already bringing many innovations to the chemical, textile, food, packaging and health care industries. It is no surprise then that academics, industry and policy makers are increasingly interested in this new technology, its economy and its contributions to a sound environment, which could make it a credible method for sustainable development.

One of the first goals on white biotechnology's agenda has been the production of biodegradable plastics. Over the past 20 years, these efforts have concentrated mainly on polyesters of 3-hydroxyacids (PHAs), which are naturally synthesized by a wide range of bacteria as an energy reserve and carbon source. These compounds have properties similar to synthetic thermoplastics and elastomers from propylene to rubber, but are completely and rapidly degraded by bacteria in soil or water. The most abundant PHA is poly(3-hydroxy-butyrate) (PHB), which bacteria synthesize from acetyl-CoA. Growing on glucose, the bacterium *Ralstonia eutropha* can amass up to 85% of its dry weight in PHB, which makes this microorganism a miniature bioplastic factory.

A major limitation of the commercialization of such bacterial plastics has always been their cost, as they are 5–10 times more expensive to produce than petroleum-based polymers. Much effort has therefore gone into reducing production costs through the development of better bacterial strains, but recently a potentially more economic and environmentally friendly alternative emerged, namely the modification of plants to synthesize PHAs. A small amount of PHB was

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first produced in *Arabidopsis thaliana* after the introduction of *R. eutropha* genes encoding two enzymes that are essential for the conversion of acetyl-CoA to PHB (Poirier *et al*., 1992). Monsanto (St Louis, MO, USA) then improved this process in 1999. Although this new wave of polymers has enormous potential, the timing of its evolution is uncertain. After initial enthusiasm, Monsanto and AstraZeneca (London, UK) abandoned these projects due to cost concerns. "Producing biopolymers from plants is a promising and fascinating scientific challenge," said Yves Poirier from the Laboratory of Plant Biotechnology at the Institute of Ecology, University of Lausanne, Switzerland. He thinks that companies are reluctant to pursue these projects because they need long-term investments that do not meet the companies' financial and time schedules. "Further genetic modifications still need to be introduced in the plants for their improvement," he said, "and once these plants are created, they will require specific harvesting and treatment protocols, with respect to regular plants. All this translates into heavy investments in new infrastructures and processing systems and into a considerable amount of time." Eight to ten years is his rough estimate of how long it will be before plant-produced PHAs might become economically viable.

Plans to manufacture a T-shirt from corn sugar have reached the same impasse. Dupont (Wilmington, DE, USA), the company that invented nylon, has for many years been developing a polymer based on 1,3-propanediol (PDO), with new levels of performance, resilience and softness. Adding an environmentally responsible dimension to the production, Dupont's polymerization plant in Decatur, Illinois (USA) has now successfully manufactured PDO from corn sugar, a renewable resource. But although their corn-based polymer, called Sorona®, is more environmentally friendly and has improved characteristics, it is again up to the markets to make it a success. "The company plans an effective shift from the petroleum-based production to the bio-based one," said Ian Hudson, Sorona® Business Director at Dupont, "but this will happen if the economic process and market demands justify the transition."

Cargill Dow (Minnetonka, MN, USA) has gone a step further. The company has developed an innovative biopolymer, NatureWorks™, which can be used to manufacture items such as clothing, packaging and office furnishings. The polymer is derived from lactic acid, which is obtained from the fermentation of corn sugar. It has already been brought to the market effectively and has recently appeared in US grocery stores as a container for organic food.

Another product that could benefit greatly from innovative biotechnology is paper. Much of the cost and considerable pollution involved in the paper-making process is caused by 'krafting', a method for removing lignin from the wood substrate. Lignin is the second most abundant polymer in nature after cellulose and provides structural stability to plants. In view of the significant economic benefits that might be achieved, many research efforts went into reducing the amount of lignin or modifying lignin structure in trees, while preserving their growth and structural integrity. Genetically modified trees with these properties already exist (Hu *et al*., 1999; Chabannes *et al*., 2001; Li *et al*., 2003), but money will probably not be made from them anytime soon. Although the paper industry could make a considerable profit by reducing production costs, no large projects in this direction have yet been undertaken. Alain Boudet, Professor at the Centre for Vegetable Biotechnology at the University Paul Sabatier (Castanet-Tolosan, France), identified two major roadblocks for the commercialization of transgenic wood. "First of all, trees with altered lignin will need more tests on their actual field performance outside the laboratory before being widely used," he explained. "Secondly, and with much more difficulty, it will be necessary to conquer the public's acceptance to yet new transgenic organisms and to the distribution of products deriving from them."

White biotechnology also concentrates on the production of energy from renewable resources and biomasses. Starch from corn, potatoes, sugar cane and wheat is already used to produce ethanol as a substitute for gasoline—Henry Ford's first car ran on ethanol. Today, some motor fuel sold in Brazil is pure ethanol derived from sugar cane, and the rest has a 20% ethanol content. In the USA, 10% of all motor fuel sold is a mixture of 90% petrol and 10% ethanol. According to the Organisation for Economic Co-operation and Development's 2001 report on biotechnology and industrial sustainability, the USA now has 58 fuel plants, which produce almost 6 billion litres of ethanol per year.

But turning starch into ethanol is neither the most environmentally nor economically efficient method, as growing plants for ethanol production involves the use of herbicides, pesticides, fertilizers, irrigation and machinery. Companies such as Novozymes (Bagsvaerd, Denmark), Genencor (Palo Alto, CA, USA) and Maxygen (Redwood City, CA, USA) are therefore exploring avenues to derive ethanol specifically from celluloid material in wood, grasses and, more attractively, agricultural waste. Much of their effort is concentrated on developing more effective bacterial cellulases that can break down agricultural waste into simple sugars to create a more plentiful and cheaper raw substrate for the production of ethanol.

Hopeful visionaries have already started to talk about a 'carbohydrate economy' replacing the old 'hydrocarbon economy'. However, "making biomass an effective feedstock is not a cheap process," reminded Kirsten Stær, Director of Stakeholder Communications at Novozymes. To get the production of biofuel up and running on a commercial basis, alongside the development of new feedstock collection systems and the creation of special production plants, a different pricing of biofuel will be required, she commented. "The price structure for fossil fuel is fixed in the market by regulatory frameworks. If the biofuel production is to be successful, it will be necessary to enforce policies that introduce subsidies to bioethanol production, for instance, or put taxes on fossil fuel production," Stær said.

This has not stopped J. Craig Venter from founding the Institute for Biological Energy Alternatives (IBEA) in Rockville, Maryland (USA) last year to advocate the production of cleaner forms of energy. IBEA recently received a US $3 million grant from the US Department of Energy, primarily to engineer an artificial microorganism to produce hydrogen. Deprived of the genes for sugar formation that normally use hydrogen ions, this organism could devote all of its energies to the production of excess hydrogen and, ideally, become a synthetic energy producer.

White biotechnology may also benefit medicine and agriculture. Vitamin B2 (riboflavin), for instance, is widely used in animal feed, human food and cosmetics

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and has traditionally been manufactured in a six-step chemical process. At BASF (Ludwigshafen, Germany), more than 1,000 tonnes of vitamin B2 are now produced per year in a single fermentation. Using the fungus *Ashbya gossypii* as a biocatalyst, BASF achieved an overall reduction in cost and environmental impact of 40%. Similarly, cephalexin, an antibiotic that is active against Gram-negative bacteria and is normally produced in a lengthy ten-step chemical synthesis, is now produced in a shorter fermentation-based process at DSM Life Sciences Products (Heerlen, The Netherlands). However, vitamin B2 is just a single success story—other vitamins and drugs are still cheaper to produce with classic organic chemistry than by innovative white biotechnology.

Nevertheless, the potential environmental benefits of shifting to biofeedstocks and bioprocesses are substantial, thinks Wolfgang Jenseit from the Institute for Applied Ecology (Freiburg, Germany). "The new bioproduction processes substitute complex chemistry reactions. This, of course, corresponds to significant energy and water savings," he explained. It also benefits the atmosphere: the carbon needed to make bioethanol from biomass was sequestered by plants from the atmosphere, so putting it back by burning ethanol does not add to global warming, Jenseit pointed out. This is certainly good news for the countries that committed to limiting greenhouse-gas emissions by ratifying the Kyoto treaty.

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And the economic benefits are expected to follow. According to the global consultancy firm McKinsey & Company, white biotechnology will occupy up to 10–20% of the entire chemical market in 2010, with annual growth rates of €11–22 billion. Huge differences exist, however, in the ways white biotechnology is managed in Europe and the USA, said Jens Riese, a Frankfurt-based Principal Associate at McKinsey & Company. "First of all, the overall sum invested in the US in the white biotech business is $250 million, a sum which by far exceeds the total European investment," he said. "Probably driven by a stronger geopolitical will of becoming independent from fossil fuel import, the US has shown a clearer propensity in the development of such technologies. Europe, on the other hand, is culturally more cautious and less adventurous in accepting innovative methodologies."

But white biotechnology has drawn interest in Europe. "There is consciousness about the need for innovation in this direction," said Oliver Wolf, Scientific Officer at the Institute for Prospective Technological Studies in Seville, Spain. "Although as yet no specific legislation exists, important steps are being taken towards the promotion of white biotechnology in Europe." White biotechnology has potentially large benefits, both economically and environmentally, for a wide range of applications. The way for its development is being paved, but it remains a relatively young technology that has to compete with a mature oil-based chemical industry that has had nearly a century to optimize its methods and production processes. Nevertheless, the growing concerns about the environment and the possibility of cheaper oil in the future make white biotechnology a serious contender.

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