# Engineering in miniature

**Biochemical factories with genetically engineered microbial 'machines' may soon be turning out fuels, plastics and medicines from municipal and other waste.**
Murdoch Mactaggart **learns of specialist research.**

**Microbes, typically single-celled organisms comprising bacteria, yeasts, algae and more, are everywhere, existing since life on earth began some three billion years ago. Bacteria are vital elements in recycling processes being responsible for the nitrogen-fixing capabilities of leguminous plants, for example, for converting carbohydrates to alcohols or breaking down oceanic oil spills and their reengineering is becoming common.**

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"Much of our emphasis is on how we can modify microbes to become more efficient cell factories." explains Merja Penttilä, Research Professor at VTT. "It's actually quite amazing what you can do through cycles of testing, modifying genetically, retesting, and so on. You can end up with microbes which are much more efficient than you would have believed at the start."

VTT is a non-profit making research institution based near Helsinki and under the aegis of a Finnish government department. Established in 1942 as a public utility, it now employs nearly 3,000 people and works with private companies and public organisations throughout the world, focussing on developing innovative solutions drawing on its multi-technology skills and experience.

## From brewing to systems biology

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"VTT's early biotechnology research was set up to serve the Finnish brewing industry" says Penttilä "and from understanding the processes and enzymes needed in beer production eventually grew into today's modern biotechnology, including systems biology and synthetic biology. It's a nice history of how you build on existing knowledge through from studies on brewing yeasts to metabolic engineering of microorganisms. VTT has always been at the forefront of innovation."

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There are now serious concerns about using food-competitive crops like maize for biofuels and VTT has long been involved in researching approaches to making bioethanol, as well as polymer precursors, from cellulose, the most common organic compound on earth and the structural component of most plants, being widely available as paper, wood, straw and fibre waste. The EU's NEMO project, in which VTT is a leading participant, focuses on using cellulosic materials in biofuel production.

"We've been working with Mascoma, a US company, in developing the techniques of consolidated bioprocessing in order to produce bioethanol efficiently from cellulosic material and to reduce the process steps." says Penttilä. "Ordinarily you have to add enzymes to hydrolyse the cellulose and then ferment the resulting sugar. By introducing genes that code for cellulases into the yeast we're getting towards a single step process. This has important cost considerations."

## Shift to biotechnology

VTT has also worked with Cargill (Nature Works) in developing

novel microbes for the production of the important bioplastic PLA, polylactic acid. "Ordinarily you'd use lactic acid bacteria but the bacteria can't tolerate low pH." adds Penttilä. "That means you have to add lime and then get rid of the resultant gypsum. However, we were able to reengineer yeasts to produce lactic acid and so contributed to this new process for turning biomass into bioplastics."

"We're still in the starting phase compared with using petrochemicals" she adds "but biotechnology is clearly a very promising technology for making fuels and chemicals. I've been surprised at just what research in this area, building on our long knowledge and experience, can achieve. Over, say, the coming twenty years I expect many chemical production processes to shift to biotechnology, probably also using urban waste resources for raw materials. What you can produce using microbes and biomass is in principle almost limitless and biorefineries could be designed each to make several different products depending on the microbes utilised."

## Conan the bacterium

The bacterial genus *Deinococcus* is highly resistant to environmental hazards such as extreme temperature or chemical environments, desiccation, or even ionising radiation. The species *D. radiodurans*, for instance, can withstand a dose of 5,000 Gy, a thousand times that which will kill a human, and genetically engineered variants are now widely used to decontaminate highly radioactive industrial sites. An interesting experiment in 2003 demonstrated that the bacterium could be used to store information following a nuclear catastrophe by translating human readable data into DNA fragments, later recovered intact.

Deinove is a French company specialising in *Deinococcus*-related applications and recently formed a research partnership with VTT in the area of cellulosic bioethanol production, already a focus of VTT's work. The project which received €8.9 million in financial support from the French state innovation agency Oséo, seeks to evaluate different *Deinococcus* species for higher yields at increased temperatures and subsequently to engineer these metabolically to improve results even more. The project also aims to reduce the input of enzymes in the process, another approach where VTT has considerable experience. Once the research is complete the process will be scaled to industrial level and a pilot test run by the sugar company Tereos.

Most *Deinococcus* bacteria have a remarkable ability to repair DNA, a mechanism studied in the case of *D. radiodurans* by a team led by Miroslav Radman, Professor of Cell Biology at Paris-Descartes University and one of the two founders of Deinove.