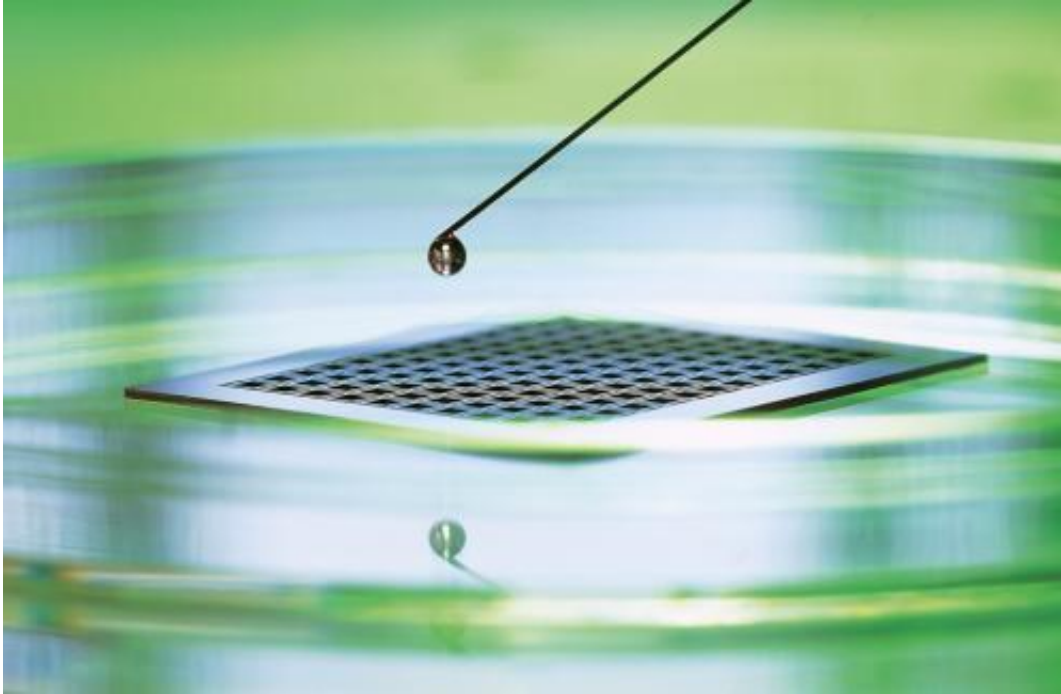


Biomolecules for the production line

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The Cell-free bioproduction could help us to produce biological ingredients more quickly and with fewer resources. Credit: Fraunhofer

To produce proteins on an industrial scale without using living cells is the ambitious goal of cell-free bioproduction. This method could help us to produce biological ingredients more quickly and with fewer resources than conventional techniques allow. Scientists and engineers from eight Fraunhofer Institutes have joined forces in an interdisciplinary research project to develop bioreactors that produce proteins without the help of intact cells. Demonstration models of the reactors will be on show to the

public for the very first time from October 8-10, 2013 at BIOTECHNICA in Hannover.

Insulin, antibodies for use in vaccines and cancer medicines, enzymes for the food, cosmetics, and detergent industries: many such substances can already be produced on a large scale using biotechnology. Currently, demand for biomolecules is often still met by making use of living [cells](#) or organisms. This involves researchers adding the gene that codes for the target [protein](#) to bacteria, yeasts, or cultures of animal or plant cells. These modified organisms are then cultivated en masse in bioreactors before the protein is finally isolated and purified. There is no doubt that the technology is very effective, but it does have disadvantages, as many of the steps in the process are costly and time-consuming. What's more, the bacteria and other cells themselves consume part of the resources to stay alive – which reduces the efficiency of the [protein synthesis](#) process. Project leader Prof. Frank Fabian Bier from the Fraunhofer Institute for Biomedical Engineering IBMT in Potsdam explains the biggest disadvantage of cell-based techniques: "Many proteins cannot be produced in cells – or else the results are very poor. Take membrane proteins, for instance, which play a major role in pharmacological research. Or proteins that poison a cell when present in high concentrations – making them potentially very useful for treating cancer."

Producing proteins without cells

Cell-free techniques do not suffer from these problems, because instead of employing intact, living cells they take only those elements of a cell needed for protein synthesis. But how does the concept of biomolecules for the production line work? First, Fraunhofer researchers must break down the cells to obtain a mixture – known as a lysate – that contains all the necessary elements for protein synthesis. Alongside enzymes, this also includes biologically active organelles and membrane parts that

synthesize the proteins according to their genetic coding. The desired genes can be added straight to the lysate; there is no longer any need for them to be implanted laboriously into the cells' DNA first.

The concept of cell-free protein synthesis has been around for a while. What the joint Fraunhofer research project seeks to do is adapt the technique for industrial production. The idea originated from the German Federal Ministry of Education and Research BMBF's Biotechnology 2020+ strategy process and is receiving 15 million euros in funding; the Fraunhofer-Gesellschaft is investing a further 6 million euros. Much has been achieved since the project was launched two years ago. The first stage was the development of automated cell harvesting and extraction techniques to produce lysates from bacteria, tobacco, and insect cells. A completely automated process supplies these lysates with amino acids and selected genetic material so that the synthesis of specific proteins can get underway.

Two bioreactor concepts

Two reactor concepts are currently undergoing testing for use in industry. One idea consists of small synthesis chambers with a partially permeable membrane through which fresh stores of ingredients for the reaction can be fed to the lysate and harmful metabolites removed. A supply and disposal system of this kind allows protein synthesis to keep going for several days. The other idea is for a microfluidic platform on which the reading of the genes and actual protein synthesis occur in separate places – in much the same way as it does in animals and plants. This system is particularly suited to lysates from animal and plant cells.

The trial reactors are the result of intensive collaboration between biologists, physicists, and mechanical and electronics engineers from the eight participating Fraunhofer Institutes. "Since the launch of the project in March 2011, we've put a tremendous amount of effort into producing

suitable lysates, establishing measurement techniques, and putting together components that can control the processes involved," stresses Prof. Bier. He concludes: "There is still a lot of scope to improve cell-free systems, and they show huge potential for making the large-scale production of important biomolecules far more economical and sparing with resources than ever before."

Provided by Fraunhofer-Gesellschaft

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