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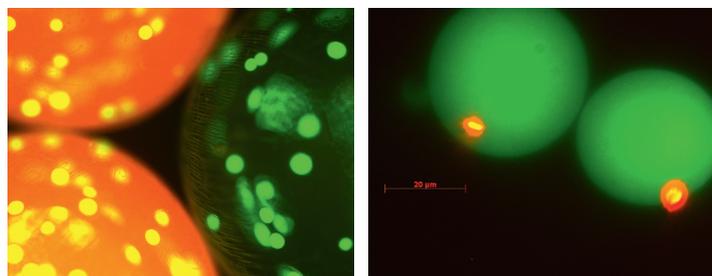
Test procedures for industrial and pharmaceutical biotechnology

## The screening millionaires

A major leap forwards: A new screening technology has made it possible to examine a million colonies of bacteria per day. The new technology is being developed by scientists at the Basel-based ETH Department of Biosystems together with the speciality chemicals company DSM. It is 100 times faster than conventional screening systems.

Efficient immobilisation of excreted products (orange) in nL reactors.

nL reactors with individual cells.



The chemicals industry is highly competitive and companies are forced to constantly improve their efficiency. Developments in biotechnology are an important catalyst in that regard. And companies often replace conventional production methods with biotechnologies. The advantages of these methods are not only economic. Biotechnological processes make use of renewable raw materials such as starches and vegetable oils, which means they have significantly less impact on the environment than petroleum-based chemical processes. Biotechnologies have been used to produce some fine chemicals for decades, and these processes are constantly being optimised.

Some vitamins have been produced using biotechnologies for years, for example. Over time, the microorganisms that produce the vitamins have developed into particularly efficient industrial strains. New developments are happening all the time: "We have a whole portfolio of projects, from small improvements to

the development of new, breakthrough technologies”, says Hans-Peter Hohmann of the Dutch speciality chemical company DSM, a leading manufacturer of vitamins.

### Unique technologies developed in Basel

One of these is a CTI-project with the Bioprocess Laboratory of the ETH's Department of Biosystems Science and Engineering (D-BSSE). Hohmann did not have to look far for a research partner. The ETH facility and the DSM subsidiary, DSM Nutritional Products, where Hohmann works are both based in the Basel area, and with good reason: Basel is home to a world-renowned biotechnology cluster. Basel's position in the world of biotechnologies is ideally suited to the CTI project. “The technology the ETH researchers are developing is unique in the world,” says Hohmann.

The technology dramatically accelerates screening, a key process in the search for even more efficient strains of bacteria. Screening is so important because it is only through this kind of systematic testing that one comes across previously unknown strains, which ideally lead to big improvements in efficiency and a significant competitive advantage.

The technology will be used to search for a new industrial strain for the production of vitamin B2, one of eight B vitamins. The worldwide market for this complex of vitamins is worth well over CHF 1 billion.

### The result of three innovations

The technology was based on an existing screening technology called flow cytometry. “Although it is fast, it was not suitable for searching for bacteria that excrete substances”, explains Martin Held, project manager at D-BSSE. The ETH researchers modified individual components of a flow cytometer with the help of the machine's manufacturer.

In addition to this, a new procedure was needed for the production of small colonies of bacteria. Since the microorganisms excrete the vitamin, there must be enough space between them to be able to determine the amount of the vitamin produced by the different versions of a bacteria. Up to now, the different versions of the bacteria were placed in small wells on special laboratory plates. The group led by Martin Held developed a procedure in which each microcolony grows in an individual bio-reactor of just a few billionths of a litre, known as a nanolitre (nl)-reactor. According to Martin Held, “in the nl-reactors, the vitamin and the bacteria that excreted it are kept together.”

The third innovation was the development of biosensors. These emit a light signal when the desired molecule, in this case the vitamin, is excreted so that it may be captured by the measuring device.

These three innovations allow incredibly quick identification and measurement of the quantity of the vitamin produced. “Our measurement device can manage up to a million colonies per day,” says Held. This is faster than existing procedures by a factor of 100.

### Uses for pharmaceutical and chemical companies

“The project is going very smoothly so far” says Oreste Ghisalba, head of CTI Biotech, who is overseeing the project as CTI Expert. He adds that the technology has another area of application. Pharmaceutical companies can benefit from the innovation as well as chemical companies. They use screening to search for new active substances. The higher capacity makes it possible to discover new, hard-to-find active substances.

“Industry has shown a high amount of interest in the technology,” says Ghisalba. Sven Panke, head of the Bioprocess Laboratory confirms, “the project with DSM is already the fourth to develop a screening technology tailored to the needs of different partners.” Among these projects, the ETH scientists have already set up a spin-off with the company FGen to develop individual applications of the screening technology for customers from industry and pharmaceuticals.

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