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Microorganisms produce nutrients in bioreactors

CO2 and H2 as starting materials for proteins and vitamins

Agricultural land needed to sustain the world's growing population is becoming increasingly scarce. To help address this challenge, researchers from the Environmental Biotechnology Group at the University of Tübingen have developed an innovative and sustainable power-to-vitamin technology. This breakthrough enables protein- and vitamin-rich foods to be produced with the help of microorganisms in a bioreactor using carbon dioxide and hydrogen.

In late 2022, the planet's population topped 8 billion.[1)] Around a third of the world's land mass is already given over to agriculture to sustain these growing numbers.[2)] 67% of this is pasture land and 32% arable.[3)] In Germany, this proportion is even higher, with nearly half of the land used for agriculture, a whopping two-thirds of which is arable farming.[4)] However, only a quarter of the latter is used to cultivate crops for direct human consumption. The rest is allocated to animal feed or renewable raw materials, primarily for biogas and biofuel production.

In 2022, German agriculture thus contributed to the release of 53.3 million tonnes of carbon dioxide equivalents (CO_2 eq.), which accounted for 7.1% of the country's total greenhouse gas emissions.[5)] Globally, the agricultural sector's share of the carbon footprint is even higher.

Bioreactors as a supplement to agriculture

Dr. Lisa Marie Schmitz and her team in the Environmental Biotechnology Group at the University of Tübingen have developed a sustainable power-to-vitamin technology. With the help of microorganisms, they produce protein- and vitamin-rich foods from carbon dioxide and hydrogen.
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A rapid shift in food production is now essential to ensure the world's population continue to have sufficient food in the future while also reducing CO_2 emissions. "We need to supplement conventional agriculture by developing additional, sustainable nutrient sources," says Dr. Lisa Marie Schmitz from the Environmental Biotechnology Group, led by Prof. Dr. Lars Angenent at the University of Tübingen's Geo and Environmental Research Centre (GUZ). "Animal protein production, in particular, consumes vast resources." In response to this, Dr. Schmitz and her team have developed an innovative process that harnesses microorganisms to produce high-quality proteins and essential micronutrients while consuming instead of emitting CO_2. "We use bioreactors that don't depend on agricultural land," she explains, highlighting the groundbreaking nature of their approach.

The new process builds on the power-to-protein technology that the research group developed several years ago. At its core is a two-step system, beginning with a specialised bioreactor where unique microorganisms - specifically *Thermoanaerobacter kivui* bacteria - are cultivated. These strictly anaerobic, acetogenic bacteria thrive without oxygen, and instead absorb CO_2 and hydrogen (H_2) from the gas phase and convert them into acetate (CH_3COO^-), the anion of acetic acid. "Their needs are remarkably minimal," explains Schmitz. "They don't require any organic material for their metabolism. Apart from a few salts and ammonium as a nitrogen source, we don't even need to add vitamins. This makes them ideally suited to fixing CO_2 and producing organic acetate that can then serve as a valuable resource for other organisms."

Acetate as a carbon source

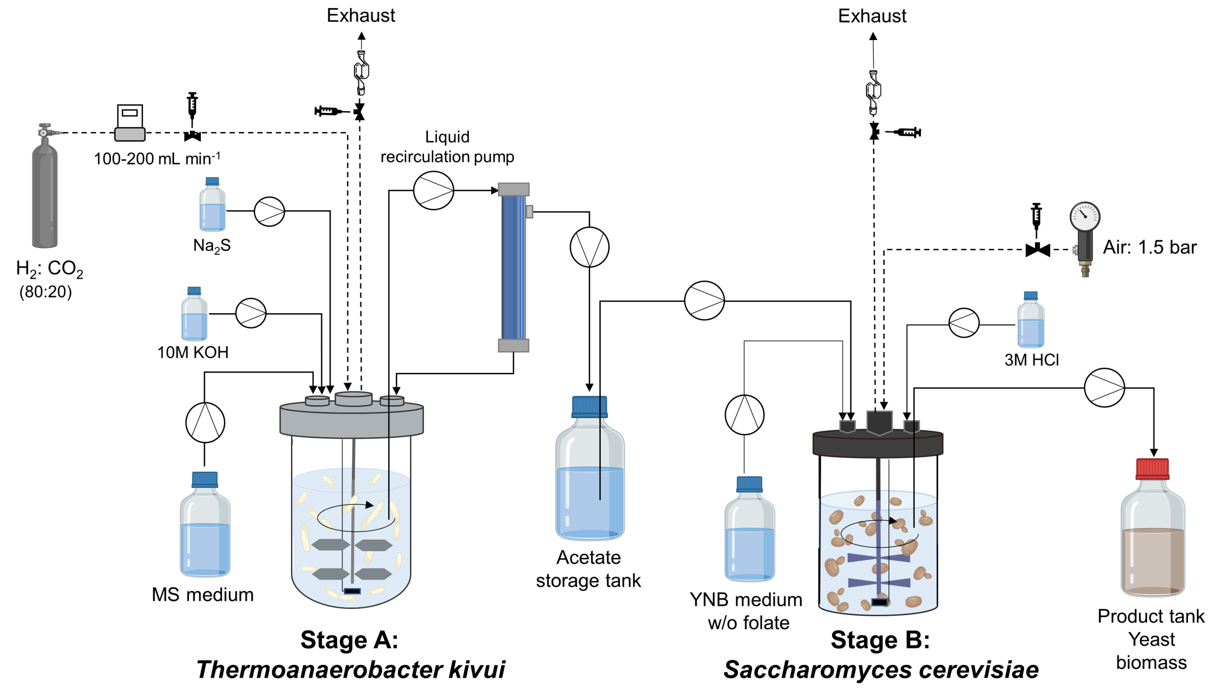
Two-stage bioreactor system on a laboratory scale. The bacterium T. kivui is cultivated in the left bioreactor and the yeast S. cerevisiae in the right. The bottle at the front contains harvested yeasts.

In a second reactor, the researchers cultivate *Saccharomyces cerevisiae*, a baker's yeast widely used in the food industry, feeding it with the sustainably produced acetate. Typically, these unicellular fungi metabolise carbohydrates such as glucose ($C_6H_{12}O_6$), but can also utilise alternative carbon sources. Inactivated yeast has long been used as a valuable food supplement in the form of yeast flakes, which is rich in proteins and essential micronutrients.[6)] "However, conventional production methods still rely on agriculture, as the glucose required is derived from plant starch," Schmitz explains. In contrast, yeast cultivated on acetate offers a significantly more efficient protein source. With a protein content of around 40 percent - higher than lentils, tuna and some kinds of meat - it offers a promising and sustainable alternative.[7)]

Yeasts produce valuable folates

Additionally, a research team led by Prof. Dr. Michael Rychlik from the Department of Analytical Food Chemistry at the Technical University of Munich analysed the folate content in the yeast - a group of compounds commonly known as vitamin B9. Folate plays a crucial role in the synthesis of nucleic acid building blocks, gene regulation and is essential for cell division and differentiation. Folate deficiency is widespread globally and can have severe consequences, particularly for foetal development during pregnancy. The studies revealed that *S. cerevisiae* produces similar amounts of folates when grown on acetate as it does in glucose-based media.[7)] The highest concentrations were observed when the yeast was cultivated in a continuous system, with two linked bioreactors. In this setup, the yeast was continuously supplied with fresh acetate while enriched biomass was simultaneously removed. Remarkably, just 6 grammes of processed yeast cells are sufficient to meet an adult's daily folate requirement, offering a promising way to combat malnutrition.

The cells in the second bioreactor similarly receive only the essential nutrients they require, such as salts, ammonium and select vitamins, but not amino acids, for example. "The less we provide, the slower *S. cerevisiae* grows. Our challenge is to find the right balance to ensure sufficient biomass production," explains Schmitz, the lead author of the study published in the journal Trends in Biotechnology. "In future, we aim to explore whether the yeast can also synthesise additional vitamins *de novo*, potentially further enhancing its nutritional value."



Schematic of the two-stage bioreactor system for producing protein- and folate-rich nutritional yeasts. The bacterium Thermoanaerobacter kivui synthesises organic acetate from CO_2 and H_2 as well as some salts and ammonium. Acetate then serves as a carbon source for the yeast fungi S. cerevisiae in a second bioreactor, enabling them to grow and produce folate. Source: L. M. Schmitz, Trends in Biotechnology, https://doi.org/10.1016/j.tibtech.2024.06.014, CC-BY 4.0 (https://creativecommons.org/licenses/by/4.0/), modified by L. M. Schmitz

Industrial production

The Environmental Biotechnology Group at the University of Tübingen is part of the Novo Nordisk Foundation CO_2 Research Centre, which focuses on mitigating climate change by developing technologies for capturing, storing and recycling CO_2.[8] As part of this international collaboration, the innovative system will soon be tested and further refined in a pilot plant in Denmark. One of the main challenges is gas fermentation in the first bioreactor - a complex process that has not yet been widely implemented in industrial facilities. Unlike CO_2, hydrogen (H_2) has very low solubility in water, requiring an efficient gas transfer process to ensure optimal microbial conversion. However, the bacteria used in this system offer a key advantage: as thermophiles, they thrive at 65°C, significantly reducing the need for cooling during production.

A techno-economic analysis revealed that this innovative food product - even according to conservative estimates - can compete with existing market alternatives on price. The cost of electricity plays a crucial role, as the electrolytic splitting of water for H_2 production is energy-intensive and so would ideally be performed using renewable sources in the future. CO_2 is currently still being purchased, but in the long run its utilisation could be financially incentivised, further improving cost efficiency. As Schmitz points out, "Our goal is not to replace traditional agriculture but to provide a sustainable supplement. This could also help increase the value of conventionally grown crops, ensuring better compensation for farmers."

Before the yeast reaches consumers, it must be dried and processed. Since it contains significant amounts of nucleic acids and hence purines - substances that can trigger gout in some individuals - as well as potential allergens, further purification is required for larger scale consumption. However, if the yeast is used merely as an additive in products such as muesli bars or yogurt, such extensive purification is not strictly necessary.

In addition to proteins and folates, nutritional yeasts contain many other essential micronutrients such as potassium, calcium, iron, zinc and almost all other B vitamins and can therefore contribute to a healthy diet. They also have a long shelf life and generate almost no waste during the production process.

"Our system offers a general platform that can be used to test acetate as a nutrient for other organisms, which then generate other end products," says Schmitz.

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Dr. Ruth Menßen-Franz

Further information

Dr. Lisa Marie Schmitz
Environmental Biotechnology Group
Geo and Environmental Research Center (GUZ)
University of Tuebingen
Schnarrenbergstraße 94-96
72076 Tübingen
Email: lisa-marie.schmitz(at)uni-tuebingen.de

- Environmental Biotechnology Group
- Schmitz Lab

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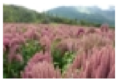

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