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Evaluating the success of biocatalysis from pharmaceuticals to environmental technology

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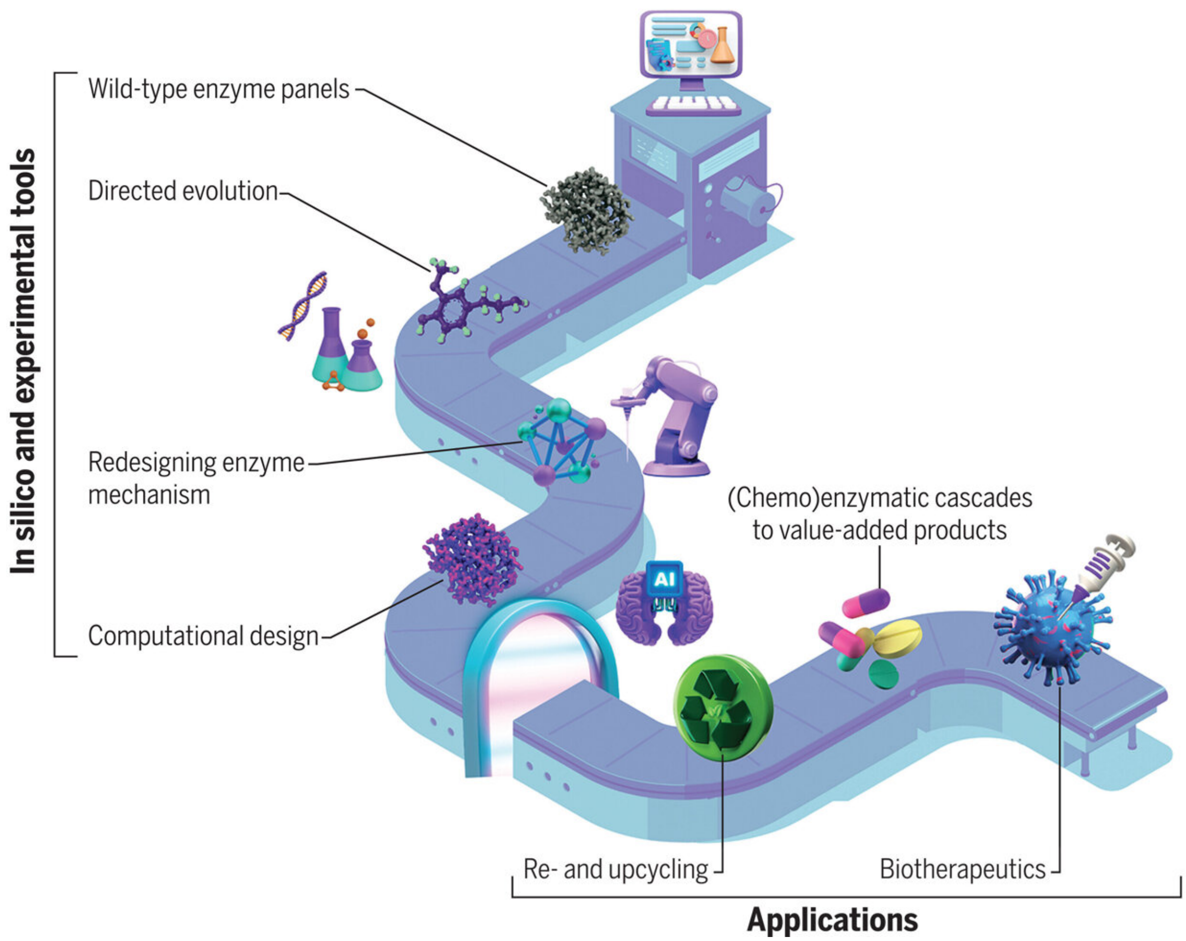

The accelerating development of biocatalysis. In silico and experimental tools developed in the last decade allow the fast creation of tailored enzymes. In addition to the concise synthesis of complex small molecules in elegant (chemo)-enzymatic cascades, newly accessible applications include enzymatic DNA synthesis, the generation of therapeutic oligonucleotides, and up- and recycling of plastic waste. [Figure created with Canva]. Credit: *Science* (2023).

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As biocatalysts, enzymes can make many chemical processes "greener" and open up promising opportunities for various industries from pharmaceuticals to environmental technology. New analytical methods, the enormous increase in data volumes and machine learning have helped boost the development of biocatalysis.

A publication in the journal *Science*, coordinated by Prof. Dr. Uwe Bornscheuer from the University of Greifswald (DE) and Prof. Dr. Rebecca Buller from the ZHAW (CH), summarizes the developments in biocatalysis.

Enzymes have been used in biocatalysis to produce semi-synthetic antibiotics, various building blocks for active pharmaceutical ingredients and basic chemicals such as acrylamide for polymers for decades.

Biocatalysis can make chemical processes more efficient, specific and energy-saving and, against the backdrop of energy shortages and climate change, is a beacon of hope for the development of greener chemistry and a comprehensive circular economy.

In the last five years, innovative and groundbreaking progress has been made in this field: Key breakthroughs have been, for example, the development of new bioinformatics tools such as machine learning, which facilitate the customized design of biocatalysts, or the possibility of equipping enzymes with the ability to carry out new chemical reactions not known from nature. It is also possible to synthesize complex molecules such as starch from the greenhouse gas carbon dioxide, by cleverly combining enzymes.

Natural enzymes are adapted to their metabolic function through evolution and must therefore be optimized for industrial applications using protein engineering methods. Although this has been done for almost three decades, important new methods have been developed in the last five years.

Not only has the number of protein sequences stored in public databases increased 20-fold, but reliable protein structures can now also be generated automatically and used together with machine learning methods to rapidly adapt biocatalysts to the requirements of an industrial process.

As a result, it is now possible to use biocatalysis to produce highly complex drug molecules such as islatravir for the treatment of AIDS or therapeutic oligonucleotides. The first author of the *Science* article, Prof. Dr. Rebecca Buller, notes that the use of enzymes is becoming a reality in an increasing number of areas. "The rapid development of bioinformatic and molecular biological methods is making the biocatalytic synthesis of increasingly complex products possible, also by teaching enzymes completely new tricks."

Enzyme to break down plastic thanks to protein engineering

The disposal of plastic waste is another global problem that can be addressed with the help of biocatalysis. In 2020, for example, protein engineering methods described a highly efficient esterase that can now be used to recycle PET plastic on an industrial scale.

"The state-of-the-art enzyme engineering methods summarized in our review should therefore make it possible to establish efficient recycling processes for other plastics in the foreseeable future," says Prof. Dr.

Uwe Bornscheuer.

The review article, written in collaboration with an international team of authors, summarizes the most important developments in biocatalysis over the last decade, which it illustrates with impressive application examples. It also ventures a look into the future of this innovative field of research.

In addition to the combination of chemical and enzymatic catalysis processes, the authors also see completely new fields of application for enzymes, for example in the production of RNA therapeutics, in gene therapy and other innovative contributions to the conservation of resources and climate protection.

More information: R. Buller et al, From nature to industry: Harnessing enzymes for biocatalysis, *Science* (2023). DOI: 10.1126/science.adh8615

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