

Enzyme Beads for More Sustainable Chemistry

Thanks to enzyme-based biocatalysis, an enormous range of pharmaceutical active ingredients and other complex molecules can be synthesized in an environmentally friendly manner. Researchers at the Karlsruhe Institute of Technology (KIT) have now developed a technology that allows to assemble enzymes into millimeter-sized, storable beads. In this process, the enzymes not only act as catalysts but also constitute the beads' material itself. In a further variant, the enzyme networks can be combined with living cells. A patent application has been filed for the technology. The results have been published in *Advanced Materials*.

In biocatalysis, enzymes are used to accelerate the reactions, instead of chemical, often toxic catalysts. This saves raw materials and energy. To ensure that this technology can be put to use as widely as possible in the chemical industry, the biocatalysts must be made available continuously and in large quantities. Moreover, they must be storable, transportable, and easy to dose. To meet all these requirements, a team headed by Professor Christof Niemeyer from KIT's Institute for Biological Interfaces 1 has refined the so-called AEH (all-enzyme hydrogels) concept. It consists in providing enzymes with complementary molecular binding modules. "When the complementary building blocks come together, they organize themselves into three-dimensional protein networks," said Niemeyer. "Thus, the enzymes are catalysts and the structural material of the beads at the same time – a great advantage over conventional methods. We avoid inactive support material, increasing the efficiency of the desired chemical reaction."

The researchers benefited from these properties to synthesize handy beads in two steps. First, they combined complementary enzyme building blocks within liquid droplets and consolidated them by rapid freezing in liquid nitrogen. Subsequent freeze-drying yielded mechanically robust, porous protein beads with defined size. The dried particles can be put into a liquid again and are then used for biocatalytic reactions.

Modular System Made from Enzymes and Cells

The team used very different enzymes and reaction types to show that the method is extremely versatile. Both individual catalytic functions and systems consisting of multiple enzymes – with or without additional additives – could be realized in the beads. "The composition of the material can be customized to suit the desired reaction," said Niemeyer. "This is some sort of modular system: We can assemble different enzyme modules to catalytic networks using defined binding molecules and subsequently transform them into a particle form that is easy to work with." The scientists also demonstrated the use of the AEH beads in continuous-flow reactors for many hours.

The team conducted further tests to combine the enzyme building blocks with cells of the *Escherichia coli* bacterium to synthesize hybrid beads. Unlike enzymes, cells are able to provide, for example, chemical energy or create intermediates. The hybrid beads remained catalytically active after more than four weeks of dry storage at room temperature. Even after having been stored for five months, the functions of the cell-enzyme systems could still be confirmed. Moreover, the researchers demonstrated that viable cells could be recovered from the materials while retaining their genetic functionality.

Target Applications: Fine Chemicals or Pharmaceuticals

"With the hybrid beads, we link two forms of biocatalysis, which are usually considered separately," said Niemeyer. "They allow us to combine individual enzymes in a targeted manner and at the same time leverage the capabilities of living cells. This yields a material that unites the two approaches and is easy to work with." Possible applications include, for example, the production of fine chemicals, flavoring agents, building blocks for pharmaceutical active ingredients, and other high-grade chemical products.

Publications

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Further information

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