

# Nanoreactors for reaction cascades

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Living cells are highly complex synthetic machines: Numerous multistep reactions run simultaneously side by side and with unbelievable efficiency and specificity. For these mainly enzymatic reactions to work so well collectively, nature makes use of a variety of concepts. One of the most important of these is division into compartments. Enzymes are not only separated spatially, but also positioned in specific locations within the cell.

Researchers from the Netherlands, led by Jan C. M. van Hest and Alan E. Rowan, have now developed an approach to copy this idea, as they report in the journal *Angewandte Chemie*.

They constructed nanoreactors by controlled positioning of two different enzymes in the central water reservoir or the plastic membrane of synthetic nanoscopic bubbles. In combination with a third enzyme in the surrounding solution, this system has made it possible to run three different enzymatic reactions simultaneously, without interference, in a “one-pot” reaction.

To mimic a cellular environment, the scientists produced nanoscopic bubbles surrounded by a membrane made of a special plastic. The plastic is a block copolymer that is analogous to a lipid, the natural building block of cell membranes, in its structure, with a water-friendly “head” and a water-repellent “tail”. In analogy to liposomes, which are made from lipids, these bubbles are called polymersomes. Thanks to nearly limitless possibilities in the production of these plastic membranes, the spectrum of properties displayed by polymersomes can be precisely

tailored.

The researchers produced their polymersomes such that they let small molecules pass through while forming a barrier to larger ones. This allows enzymes to be trapped inside the polymersomes (in the water reservoir) while the smaller substrate or product molecules pass through unhindered.

To demonstrate the potential of their “nanoreactors”, the researchers bound the enzyme horseradish peroxidase into the membrane itself. Within the water reservoir, they trapped the enzyme glucose oxidase. The surrounding solution contained the enzyme lipase B. Glucose molecules with four acetyl groups attached were added as the substrate. In the first step, the lipase B split off the acetyl groups. The resulting glucose could cross the membrane, where it encountered the glucose oxidase and was oxidized by it. This reaction formed hydrogen peroxide, which is just what the horseradish peroxidase was waiting for in order to convert the sample substrate ABTS (2,2'-azinobis(3-ethylbenzthiazoline-6-sulfonic acid))—also contained in the solution—into its radical cation.

Citation: Jan C. M. van Hest, Positional Assembly of Enzymes in Polymersome Nanoreactors for Cascade Reactions, *Angewandte Chemie International Edition*, doi: 10.1002/anie.200701125

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