Switchable nanovalves: pH-sensitive pseudorotaxane as reversible gate for drug nanotransporter

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We encounter valves every day, whether in the water faucet, the carburetor in our car, or our bicycle tire tube. Valves are also present in the world of nanotechnology.

A team of researchers headed by J. Fraser Stoddart and Jeffrey I. Zink at the University of California, Los Angeles, has now developed a new nanovalve. In the journal *Angewandte Chemie*, the scientists reveal what is special about it: In contrast to prior versions, which only function in organic solvents, this valve operates in an aqueous environment and under physiological conditions—prerequisites for any application as a gate for nanoscopic drug-transport agents, which need to set their cargo free at the right place and time.

In order for pharmaceuticals to affect only the target diseased organ, suitable nanopackaging is required to bring the drug to the target area and release it only there. One example of a good nanoscopic packaging agent is a tiny sphere of porous silica. Its pores can be filled with the drug and closed with tiny controllable valves.

The scientists attached stem-shaped molecules onto the surface of the porous spheres and filled the pores with guest molecules. At neutral to acidic pH values, they stacked cucurbituril molecules onto these “stems”. Cucurbituril is a fat, ring-shaped molecule reminiscent of a pumpkin that has both ends hollowed out. The resulting supramolecular structure,

which resembles a skewered pumpkin and is known to chemists as a pseudorotaxane, blocks the pores, so that the guest molecules cannot exit. The nanovalve is closed.

If the pH value is raised into the basic range, however, the interaction between the “pumpkins” and the “skewers” is weakened, and the pumpkins come off, opening the pores. Now the valves are open and the guest molecules can exit.

At this point the molecular details of the individual components still need to be tweaked. The goal: very small differences in pH values between healthy and diseased tissue should be sufficient to switch the valves and release the drug only in diseased cells.

Citation: Jeffrey I. Zink, pH-Responsive Supramolecular Nanovalves Based on Cucurbit[6]uril Pseudorotaxanes, *Angewandte Chemie International Edition* 2008, 47, No. 12, 2222–2226, doi: 10.1002/anie.200705211

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