

Tiny tools aren't toys

Enzyme-based machinery could have medical applications

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Researchers have created millimeter-sized metal tools that contort on command, clamping shut or popping open in response to specific chemical cues. The smart devices, described online September 17 in the *Journal of the American Chemical Society*, may one day be used to biopsy a liver, prop open an artery or deliver drugs to a target site.

Even tiny tools need some power source — a battery pack or electrical wires — but that adds unwanted bulk, says study leader David Gracias of Johns Hopkins University in Baltimore. Yet nature is filled with minimachines: muscles contract, leaves turn to the sun, a Venus fly trap snaps shut. “In nature, and in us, these respond to chemistry,” Gracias says.

It took some doing to make devices that could respond to chemicals in the right time and place, yet were still friendly inside the body. Gracias and his team began with thin silicon wafers and coated them with layers of chromium, nickel and gold. Using a high-tech version of a stencil, the researchers patterned the metal



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TIGHT GRIP

Tiny tools that may one day deliver or collect things in the body are built in an open position (far left) but snap shut when triggered with enzymes (left to right).

D. Gracias et al/JACS 2010

layers into parts that looked like a flower or open palm of the hand. They added hinges so the open hand could clamp shut.

Then they added layers of biologically friendly polymers that break down in the presence of enzymes. By layering these polymers just right the researchers could selectively degrade them, prompting the clamp to spring shut or pop open.

One polymer was derived from collagen, the connective tissue that holds a lot of the body together. The other was derived from cellulose, the stuff of plant cell walls.

Both collagen and cellulose get chewed up by specific enzymes. Cellulases, which are made by fungi and bacteria, destroy cellulose and allow termites to chew through wood.

Proteases, which break down meat in human stomachs, take apart collagen. Certain tumors are protease factories, Gracias says, raising the possibility that minimachines might be designed to trigger automatically upon reaching diseased tissue.

"It is very creative work," says biomedical engineer Kam Leong of Duke University in Durham, N.C., who was not part of the research. "The proof of principle is fascinating."

To test their claspers the team made some fake innards from resin and embedded some hard-to-reach bird liver tissue inside. Using a magnet, they piloted the claspers through the faux bile duct and into the liver. Then they added cellulase with a syringe. The gripper closed around the bit of bird tissue. Then the team piloted the grippers back out with a magnet, having performed a rough version of a biopsy.

The grippers also retrieved a small bead from the digestive tract of their model and delivered it to the liver.

There is much work to be done before the minitools are used in real bodies for real problems, says Leong. "The ultimate test will be in vivo, but this is an important contribution."

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