ACS MEETING NEWS

Steering nanomotors toward applications

Tiny machines are revved up to leave the lab, but they face roadblocks

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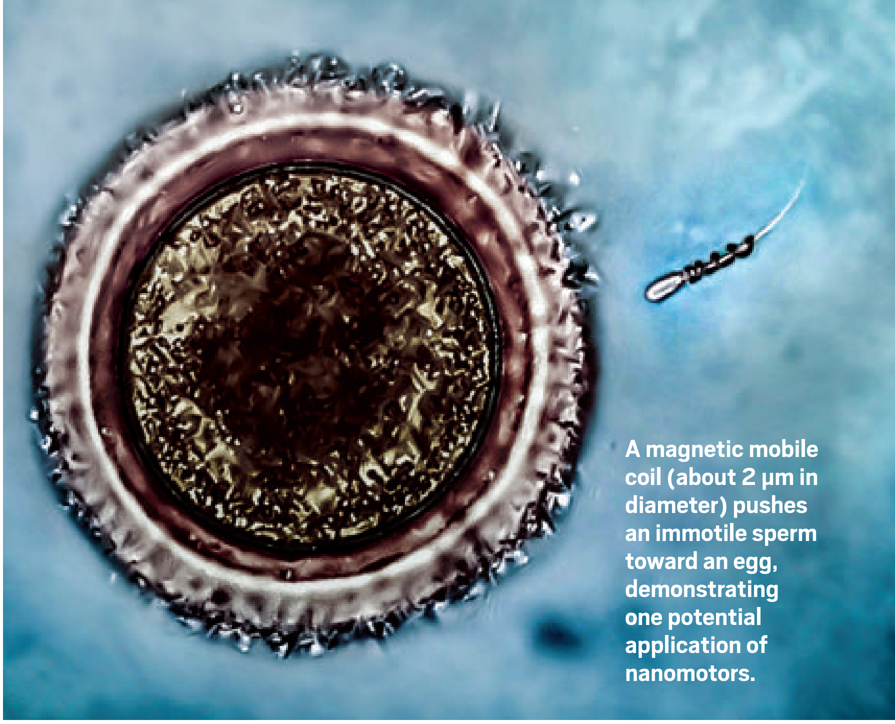


A magnetic mobile coil (about 2 µm in diameter) pushes an immotile sperm toward an egg, demonstrating one potential application of nanomotors.

NANO. LETT.

Everyone's done it. Joseph Wang just had the bad luck of having a couple reporters riding along for a trip to his lab when it happened.

The head of nanoengineering at the University of California, San Diego, was driving along the coast on a crisp, sun-buttered morning and realized he needed to change lanes. He started veering right, saw an approaching Range Rover, and swerved back into his lane.

Wang waved contritely and apologized through an open window as the Range Rover passed, its driver honking and cursing. The scene might have been a cliché for Southern California, but it was also a suitable metaphor for Wang's field of expertise: Nanomotors are racing forward, but obstacles block their path.

Wang and his group have long been leaders in developing applications for these tiny, engineered motile particles, and researchers worldwide are now using the motors to chase goals including drug delivery, environmental cleanup, and even overcoming male infertility. Over the past decade, scientists have devised many ways to power and control these motors, which usually have at least one nanoscale dimension, in the lab. But there's also a growing sense among these researchers that they'll need to propel these machines into real-world applications soon to keep their peers, the public, and funding agencies interested in their work.

Simplistically speaking, nanomotors can swim in two environments: inside living things, and outside living things. The first venue represents the long-range goal of the field, Wang said, sitting on a bench at the ACS national meeting in San Diego last month. The goal harkens back to the classic 1966 science-fiction film "Fantastic Voyage," he explained. People dream of being able to shrink machines and have them swim inside bodies to combat disease. But this is a ways off, Wang said, and motors could find more immediate uses outside the body.

Wang's team showcased examples of motors in both settings at the San Diego meeting. Attendees at one talk watched hydrogen peroxide-fueled gold nanoparticles with hemispherical platinum coatings drive themselves into cracks in electronic circuits to restore conductivity (*Nano Lett.* 2015, DOI: 10.1021/acs.nanolett.5b03140).

The two metals of these Janus particles, named after the two-faced Roman god, possess different catalytic properties and create a chemical gradient in their immediate vicinity. This gradient gives rise to an electric field that propels the particles.

In another talk, audience members learned how Wang's team, working with UCSD nanoengineer Liangfang Zhang, put motors inside living beings—specifically mice—for the first time (*ACS Nano* 2015, DOI: 10.1021/nn507097k). The team made nanomotors from polymer-wrapped zinc and fed them to mice in the lab. The micrometer-scale motors, which carry gold nanoparticles as cargo, didn't turn on until they reached a mouse's stomach, where the acid reacted with zinc to generate hydrogen bubbles that propelled the rods like torpedoes.

Stomachs torpedoed by zinc motors were dosed with more gold nanoparticles more quickly and retained those particles better than stomachs treated with cargo-carrying particles propelled by diffusion. Although the researchers used gold nanoparticles in these experiments, they are working to develop motors that deliver therapeutics and more.

"We ultimately want to have particles that drive to a tumor, image it, treat it, and then biodegrade completely," Wang explained. But this will take time.

In the meantime, nanomotorists may benefit from keeping their designs simple when it comes to biomedical applications, suggested Raj Bawa, a patent agent at the law firm Bawa Biotech and a scientific adviser to Teva Pharmaceutical Industries. These devices blur the distinction between chemical and mechanical action, making it harder for regulatory agencies, such as the Food & Drug Administration, to classify the motors according to conventional criteria, he said.

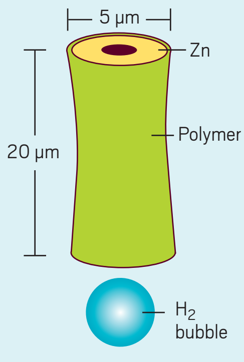
FDA, for instance, differentiates between drugs and devices, but what evidence does it have that a self-propelled nanoparticle loaded with a therapeutic behaves like one and not the other? "Governmental regulatory bodies lack regulatory and technical knowledge on these motors," Bawa told C&EN by phone. "The clinical trial route will be interesting, to say the least."

But Samuel Sánchez, a group leader at the Institute of Catalonia and the Max Planck Institute for Intelligent Systems, said that he doesn't see regulators as the largest obstacle to nanomotor development. He thinks his peers researching more conventional, passive methods of drug delivery,

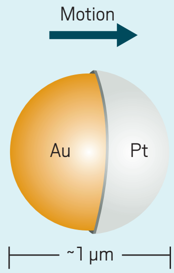
Nanomotorin’

An illustrative but incomplete guide to propulsion methods and motors

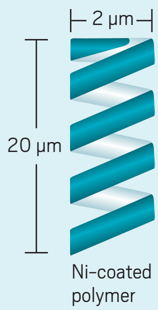
What makes it go?
Bubbles
How does it work?
Materials in a motor react with chemical fuel in its environment to generate gas bubbles that send the motor swimming like a torpedo.
Where has it gone lately?
Zinc-filled microcylinders torpedoed themselves into the stomach tissue of mice, thanks to hydrogen bubbles that evolve when the metal reacted with stomach acid.[a]



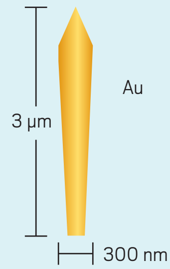
What makes it go?
Self-electrophoresis
How does it work?
Rods or spheres made from multiple metals create chemical concentration gradients thanks to their asymmetric catalytic properties. The gradients create local electric fields that propel the motors.
Where has it gone lately?
Janus particles made from gold and platinum propelled themselves into cracks in circuits to repair electronics.[b]



What makes it go?
Magnetic fields
How does it work?
Researchers can steer particles made using magnetic metals with magnetic fields.
Where has it gone lately?
Researchers mobilized immotile but otherwise healthy sperm with the help of magnetic microhelices.[c]



What makes it go?
Acoustic energy
How does it work?
Waves generated by ultrasound can drive asymmetrically shaped particles.
Where has it gone lately?
Ultrasound allowed researchers to drive gold nanomotors around inside cells for the first time in 2014.[d]



Note: Dimensions shown are specific to application described. **a** *ACS Nano* 2015, DOI: 10.1021/nn507097k. **b** *Nano Lett.* 2015, DOI: 10.1021/acs.nanolett.5b03140. **c** *Nano Lett.* 2016, DOI: 10.1021/acs.nanolett.5b04221. **d** *Angew. Chem. Int. Ed.* 2014, DOI: 10.1002/anie.201309629. **Source**: Adapted from the Wang group and C&EN

such as liposomal packaging used in nanomedicines, could pose more resistance.

“They’re going to ask, ‘Are the motors better than what we already have, or do they just look fancier?’ ” Sánchez said. “We cannot keep hypothesizing or claiming they are going to be extraordinary, novel, and disruptive. They are. But have we proven anything?” he asked. “Not yet. And we need to hurry up.”

If drug developers and financiers aren’t convinced the motors can offer substantial benefits to passively diffusing drugs, the field could struggle to advance, Sánchez said. He added that he’s encouraged by recent progress in the field, though. Researchers have inserted these motors into cancer cells. And his own group has invented biodegradable silica Janus particles fueled by glucose and urea—both in ample supply inside people’s bodies—rather than hydrogen peroxide.

Still, Sánchez recognizes the utility of nanomotors in applications outside the body, particularly in cleaning dirty water (*Nano Lett.* 2016, DOI: 10.1021/acs.nanolett.6b00768). Active motors can scrub solutions at up to 100 times the speed of chemical treatments that rely on diffusion, Wang said in San Diego.

In 2013, Sánchez was part of a team that showed that rolled-up bilayers of iron and platinum could propel themselves through dilute hydrogen peroxide solutions while simultaneously oxidizing and degrading organic pollutants. Sánchez now has funding from the European Commission to run a proof-of-concept project to assess how to bring these motors to market.

The motors are expensive, but researchers can mass-produce them with standard procedures borrowed from the microelectronics industry, and the motors are reusable, Sánchez said. He envisions that, in the near future, textile companies, for instance, could use nanomotors to clean dyes from wastewater, rather than shipping it to a treatment plant.

Oliver G. Schmidt, who led the 2013 water-cleaning project, agreed that this is an interesting application—in fact, his team recently developed more eco-friendly motors for the task (*Nano Lett.* 2016, DOI: 10.1021/acs.nanolett.5b05032). But he's unsure whether researchers will be able to create enough motors economically to treat metric tons of water. Schmidt, a material scientist at the Leibniz Institute for Solid State & Materials Research, is also researching other applications for nanomotors, however, and recently generated substantial media buzz with his group's "spermbots."

His team used a technique known as three-dimensional laser writing to create helical polymer microstructures. A subsequent nickel coating made the helices magnetic. The researchers added the helices into a suspension with healthy but immotile sperm—often the culprits in male infertility—and maneuvered one of the magnetic motors to thread a stationary sperm's tail through the center of the helix. The team could then drive the engineered and natural swimmer together and deliver the sperm to an egg.

Schmidt admitted it will be years before this is a viable in vivo treatment for infertility. One of the biggest challenges will be imaging a helix-sperm duo inside a body, but this is a problem for any motor destined for the body, he said. Still, his approach highlights two emerging ideas that could help nanomotors progress to real-world applications more quickly.

First, the hybrid system takes advantage of biological functions. Helping living cells do what they naturally do can lessen the responsibility shouldered by a motor and the engineering that goes into it. The second idea is about being selective. "There is not one motor for every application," Schmidt said. "So I think you have to be very careful in selecting an application."

By choosing a specific application, researchers can focus on optimizing the motor for it. Years ago, groups may have taken more of a scattershot approach, throwing many motors at many problems, but Schmidt said the field has matured in its focus.

About four years ago, Wang, Schmidt, and Sánchez organized a nanomotor conference in Dresden and invited Geoffrey A. Ozin to deliver the opening keynote lecture. Ozin, sometimes referred to as the father of nanochemistry, independently invented catalytic nanomotors concurrently with Pennsylvania State University's pioneering nanomotor authorities, Thomas E. Mallouk and Ayusman Sen (*Chem Commun.* 2005, DOI: 10.1039/B414896G; *J. Am. Chem. Soc.* 2004, DOI: 10.1021/ja047697z, respectively).

At the time, Ozin wasn't confident that a career in nanomotors would be sustainable for his students. So he decided to move "on to bigger things, like trying to save the human race," he said, pointing to his current work converting carbon dioxide to fuel. But watching from the sidelines, he has been impressed with the nanomotor field, its leaders, and a number of potential applications.

Now, Ozin said, he could believe in a career in nanomotors. "I expect chemically powered nanomotor industries to emerge in the not-too-distant future." ■