NANOTECHNOLOGY

Borrowing From Biology to Power the Petite

Nanotechnology researchers are harvesting molecular motors from cells in hopes of using them to drive nano-sized devices

If you received a molecule-sized car, snowmobile, or jet ski for Christmas, you've probably realized by now that the thing is totally useless. It just sits there on your microscope slide like an inert dust speck, incapable of going for a spin around the cover slip. Okay, so molecular vehicles are pure fantasy. But their immobility is a problem that's all too real for would-be builders of nano-sized devices. Such devices are so small, there's no obvious way to power them. Now, researchers are turning to biology for what may be a possible solution: molecular motors from living things.

Cells are packed with protein-based motors powered by the chemical fuel of life, adenosine triphosphate, or ATP. These motors ferry cargo, flex muscles, and even copy DNA. And at a recent meeting,* two groups, one led by Carlo Montemagno of Cornell University in Ithaca, New York, and the other by Viola Vogel of the University of Washington in Seattle, reported taking the first baby steps toward harnessing these motors to power nanotechnology devices. Like molecular mechanics, the researchers have unbolted the motors from their cellular moorings, remounted them on engineered surfaces, and demonstrated that they can in fact perform work, such as twirling microscopic plastic beads. "What we're really trying to do is make engineered systems that tap into the energy system of life," says Montemagno.

The effort still has a long way to go. But the early work is already generating enthusiasm in the community. "I think it's a very productive path to follow," says Al Globus, a nanotechnology expert at the National Aeronautics and Space Administration's Ames Research Center, Moffat Field, California. If the effort does pan out, it could help researchers make everything from tiny pumps that release lifesaving drugs when needed to futuristic materials that heal themselves when damaged.

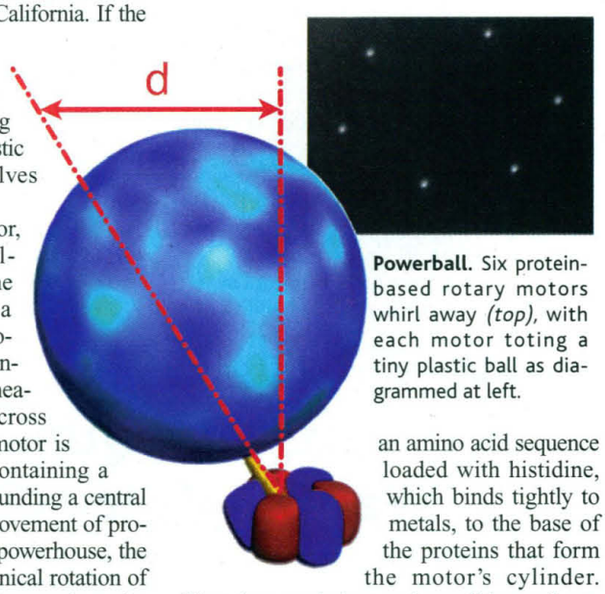
For their molecular motor, Montemagno and his colleagues turned to one of the cell's heavy lifters: ATPase, a complex of nine types of proteins that work together to generate ATP. While tiny—it measures just 12 nanometers across and 12 high—this cellular motor is remarkably sophisticated, containing a cylinder of six proteins surrounding a central shaft. ATPase converts the movement of protons within the cell's energy powerhouse, the mitochondrion, into a mechanical rotation of the shaft, a motion that helps catalyze the formation of ATP. But the motor can also run in reverse, burning ATPs to rotate the shaft and move protons.

Last year, Hiroyuki Noji and his colleagues at the Tokyo Institute of Technology and Keio University in Yokohama, Japan, captured this rotational motion on camera for the first time (see *Science*, 4 December, p. 1844). They dangled a fluorescent-tagged molecule off the end of the shaft, fed the motor ATP, then put it through a microscope and took sequential pictures of the shaft as it rotated in circles around the cylinder.

Based on the number of rotations produced by a given amount of ATP, the researchers calculated that the motor operates at near 100% efficiency— "well above the efficiency of motors we're capable of building," says Montemagno. "If the motor was as big as a person, it would be able to spin a telephone pole about 2 kilometers long about one revolution per second."

That result inspired Montemagno and his Cornell colleagues—George Bachand, Scott Stelick, and Marlene Bachand—to see if they could use the ATPase rotary motor to move man-made objects. They started by genetically engineering two changes into ATPase proteins, one to stick the motors to metal surfaces and the other to provide an attachment site for the beads that they wanted the motor to move.

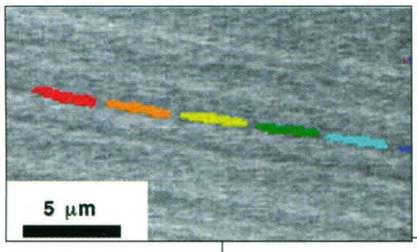
To make the first change, the team added an amino acid sequence loaded with histidine, which binds tightly to metals, to the base of the proteins that form the motor's cylinder. Next they used electron beam lithography to pattern an array of nickel islands—each roughly 40 nanometers across—atop a glass microscope cover slip. When they then spritzed water on top to keep the proteins happy and added the motors, the base of the cylinders bound to the nickel islands, causing the motors to stand upright.

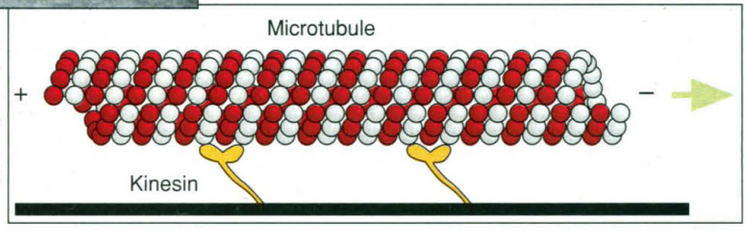


Powerball. Six protein-based rotary motors whirl away *(top)*, with each motor toting a tiny plastic ball as diagrammed at left.

To attach the beads, which were made of plastic or a plastic/iron composite and coated with a small organic molecule called biotin, Montemagno and his colleagues added cystine, a sulfur-containing amino acid, to the top of the central shaft. That allowed the shaft to grab a small sulfur-binding protein called streptavidin, which could in turn bind the biotin-coated beads. When the researchers then added ATP fuel to the solution atop the slide and used a laser-based interferometer to track the beads' movement, they could see their array of motors twirling in endless loops, like a dance floor of nano-sized dervishes. "I had the thing running for well over 2

*Sixth Foresight Conference on Molecular Nanotechnology, Santa Clara, California, 13 to 15 November 1998.





On track. As shown at right, kinesin motor proteins shuttle microtubules down a grove in a plastic film, with colors marking 5-second intervals *(top)*.

CREDITS: (TOP) C. MONTEMAGNO *ET AL.*, *NANOTECHNOLOGY*, IN PRESS; (BOTTOM) V. VOGEL, UNIVERSITY OF WASHINGTON

hours at a time," says Montemagno. "It was seriously cool."

But whirling beads—impressive as they may be—are still a long way from nanorobots rooting through the body. So Montemagno's team is pressing ahead. They're currently working on replacing the beads with tiny magnetic bars. If the motors spin the bars, the researchers will be able to measure precisely how strong the motors are by applying an outside magnetic field: By increasing the field until the motors can no longer spin, they will be able to probe the limit of the motor's power.

What's more, the spinning bars should generate an electrical current that might eventually be used to power devices, such as chip-based drug delivery pumps or chemical weapons sensors implanted in the body. But these uses, Montemagno says, are just the beginning. "There's 100,000 different things you could do with these motors," he says.

Washington's Vogel says much the same thing about her team's contraption, a nanoscale monorail in which a collection of molecular motors all lined up on a surface pass a tiny tube hand over hand down the line. Vogel based her monorail on one of the cell's own transport systems, which consists of tracks made of microtubules, tube-shaped assemblies of a protein called tubulin, and small motors made of another protein, kinesin. In cells, the kinesin motors latch onto the fixed microtubules and churn like steam engines from one end of the line to the other, ferrying molecular cargo such as proteins and lipids. But for their experiment, Vogel and her colleagues John Dennis and Jonathan Howard reversed these roles, fastening kinesin motors to a surface and having them shuttle microtubules down the line from one motor to the next.

Biophysicists studying kinesin motors had done related experiments in the past. But in those, Vogel says, the kinesins were in random locations on surfaces. When microtubules and ATP were then added, the kinesins shuttled microtubules in all directions. To control the transport, the Washington team had to line up the kinesins. Here, the researchers took a low-tech approach. They simply rubbed a block of polytetrafluoroethylene, or PFTE, across a glass slide, causing molecules of the chainlike polymers to rub off and coat it. The scraping acted something like a hair brush, getting all the PFTE chains to line up on the surface, creating a series of grooves running for micrometers along the slide.

After submerging the slides in water and coating them with a small protein called casein, to protect overlying proteins, they added the kinesin motors, which settled into the grooves. They then sprinkled on a few microtubules, which were tagged with fluorescent compounds so they could be seen, and dropped some ATP fuel into the solution.

By turning on a xenon lamp to set the microtubules aglow and letting their cameras roll, Vogel and her colleagues could see the kinesins push their tubular cargo in one direction, moving it hand over hand down the parallel grooves. "Even though kinesins move on the nanoscale, we could watch the microtubules move on the micron scale," says Vogel.

For now, the team is using the monorail to study the performance of their motors. But down the road, Vogel says that the tiny rail lines could be used to transport replacement components for self-healing biomaterials for medical implants. If this and other efforts to motorize the nanoworld are successful, those microscope slides may soon see their first traffic jams. **–ROBERT F. SERVICE**

MEETING AMERICAN GEOPHYSICAL UNION

From Eastern Quakes to a Warming's Icy Clues

SAN FRANCISCO—A record 8300 researchers gathered here on 6 to 10 December for the fall meeting of the American Geophysical Union. At this smorgasbord of earth and planetary science, the topics ranged from the future of giant earthquakes in southeastern Missouri to evidence that ancient climate changes took place in lockstep in the tropics and Greenland.

No More New Madrid Quakes?

Residents of what is now southeastern Missouri suffered through the horrific winter of 1811–12, devastated not by the weather but by the Earth itself: Between December and February, the three largest earthquakes to hit eastern North America in historic times destroyed the town of New Madrid. The most violent of the quakes—which rivaled any quake in California—momentarily reversed the flow of the Mississippi River, shot plumes of sand and water 10 meters in the air, and rang church bells 1000 kilometers away in Charleston. Ever since, scientists have wondered when the next New Madrid quake will strike, and a 1992 study suggested it might be soon—in the next few hundred years. But at the meeting, geophysicists monitoring the New Madrid region for signs of strain reported that the next big jolt shouldn't hit for 5000 or 10,000 years, if then.

"I think we've vastly overestimated the seismic hazard of New Madrid," says geophysicist Seth Stein of Northwestern University in Evanston, Illinois, who led a group that has surveyed the area for the past 6 years. A damaging but smaller quake is still possible, says Stein, but "the hazard of large earthquakes is very, very small." Not everyone is quite so confident. Because geophysicists don't really understand why the New Madrid faults ruptured in the first place, notes Paul Segall of Stanford University, another magnitude 7 to 8 "can't be dismissed at this point. ... The simplest assumption is, if [big quakes] happened in the past, they can happen in the future."

The last quake's mark. A spit of dry land juts above flood waters in a bend of the Mississippi, shoved there by the 1812 quake.

CREDIT: ARCH C. JOHNSTON

The new results come from satellite-based searches for movement of the land above the buried faults that zigzag across far southeastern Missouri, Tennessee, and Arkansas. If stress is building up along a locked fault, driving it toward eventual rupture in a large quake, the land on either side should be deforming, shifting the surface in opposite directions. Researchers can detect such subtle motions—a few millimeters per year across tens of kilometers—using the Global Positioning System (GPS), an array of military satellites in precisely known orbits. By comparing minute differences in arrival times of a satellite's radio signal at two sites, the distance between markers tens of kilometers apart can be determined to within a few millimeters. Researchers repeat the measurements over a period of years to spot movement of the markers and the ground.

After conducting GPS surveys of 24 sites