Imagine that we could make cars, aircraft and submarines as small as bacteria or molecules. Microscopic robotic surgeons, injected in the body, could locate and neutralize the causes of disease—for example, the plaque inside arteries or the protein deposits that may cause Alzheimer’s disease. And nanomachines—robots having features and components at the nanometer scale—could penetrate the steel beams of bridges or the wings of airplanes, fixing invisible cracks before they propagate and cause catastrophic failures.

In recent years chemists have created an array of remarkable molecular-scale structures that could become parts of minute machines. James Tour and his co-workers at Rice University, for instance, have synthesized a molecular-scale car that features as wheels four buckyballs (carbon molecules shaped like soccer balls), 5,000 times as small as a human cell.

But look under the hood of the nanocar, and you will not find an engine. Tour’s nanocars so far move only insofar as they are jostled by random collisions with the molecules around them, a process known as Brownian motion. This is the biggest current problem with molecular machines: we know how to build them, but we still do not know how to power them.

At the scales of living cells or smaller, that task poses some unique challenges. Air and water feel as thick as molasses, and Brownian motion militates against forcing molecules to move in precise ways. In such conditions, nanoscale versions of motors such as those that power cars or hair dryers—assuming that we knew how to build them that small—could never even start.

Nature, in contrast, provides many examples of nanomotors. To see the things they can do, one need only look at a living cell. The cell uses nanoengines to change its shape, push apart its chromosomes as it divides, construct proteins, engulf nutrients, shuttle chemicals around, and so on. All these motors, as well as those that power muscle contractions and the corkscrew motion of bacterial flagella, are based on the same principle: they convert chemical energy—usually stored as adenosine triphosphate, or ATP—into mechanical energy. And all exploit catalysts, compounds able to facilitate chemical reactions such as the breakdown of ATP. Researchers are now making exciting progress toward building artificial nanomotors by applying similar principles.

In 2004 we were part of a team at Pennsylvania State University that developed simple nanomotors that catalytically con-
vert the energy stored in fuel molecules into motion. We took inspiration from a considerably larger catalytic motor reported in 2002 by Rustem Ismagilov and George Whitesides, both at Harvard University. The Harvard team had found that centimeter-scale “boats” with catalytic platinum strips on their stern would spontaneously move on the surface of a tank of water and hydrogen peroxide (H₂O₂). The platinum promoted the breakup of H₂O₂ into oxygen and water, and bubbles of oxygen formed that seemed to push the boats ahead by recoil, the way the exhaust coming out the back of a rocket gives it forward thrust.

Credible Shrinking
Our miniaturized version of the Harvard engine was a gold-platinum rod about as long as a bacterial cell (two microns) and half as wide (350 nanometers). Our rods were mixed into the solution, rather than floating on the surface. Like the ATP-powered molecular motors inside the cell, these tiny catalytic cylinders were essentially immersed in their own fuel. And they did indeed move autonomously, at speeds of tens of microns per second, bearing an eerie resemblance under the microscope to live swimming bacteria [see video at www.SciAm.com/nanomotor].

As often happens in science, however, the hypothesis that led to the experiment was wrong. We had imagined our nanorods spewing tiny bubbles off their back and being pushed along by recoil. But what they actually do is more interesting, because it reminds nanotechnologists that we must think very differently about motion on small length scales.

At the macroscale, the notion of recoil makes good sense. When someone swims or rows a boat, their arms, legs or oars push water backward, and the recoil force pushes the body or boat forward. In this way, a swimmer or boat can glide forward even after one stops pushing. How far an object glides is determined by the viscous force, or drag, and by the inertia, a body’s resistance to changes in its velocity. The drag is proportional to the object’s width, whereas the inertia is proportional to the object’s mass, which in turn is proportional to the width to the third power. For smaller objects, inertia scales down much faster than drag, becoming negligible, so that drag wins out. On the micron scale, any gliding ends in about one microsecond, and the glide distance is less than one 100th of a nanometer. Hence, for a micron-size body in water, swimming is a bit like wading through honey. A nanomotor has no memory of anything that pushed on it—no inertia—and inertial propulsion schemes (such as drifting...
after the recoil from bubbles) are hopeless.

The way our nanorods actually work is that they apply a continuous force to prevail over the drag with no need for gliding. At the platinum end, each \( \text{H}_2\text{O}_2 \) molecule is broken down into an oxygen molecule, two electrons and two protons. At the gold end, electrons and protons combine with each \( \text{H}_2\text{O}_2 \) molecule to produce two water molecules. These reactions generate an excess of protons at one end of the rod and a dearth of protons at the other end; consequently, the protons must move from platinum to gold along the surface of the rod.

Like all positive ions in water, protons attract the negatively charged regions of water molecules and thus drag water molecules along as they move, propelling the rod in the opposite direction [see box on opposite page], as dictated by Newton’s law of motion that every action has an equal and opposite reaction.

Once this principle was established (with the help of our students and our Penn State collaborators Vincent H. Crespi, Darrell Velegol and Jeffrey Catchmark), several other catalytic nanomotor designs followed. And Adam Heller’s research group at the University of Texas at Austin and Joseph Wang’s group at Arizona State University showed that mixtures of different fuels—glucose and oxygen or \( \text{H}_2\text{O}_2 \) and hydrazine—could make motors run faster than they do with a single fuel.

Whereas freely suspended metal nanorods move with respect to the bulk solution, an immobilized metal structure in the presence of \( \text{H}_2\text{O}_2 \) will induce fluid flows at the interface between the structure and the fluid, thereby potentially powering the motion of something else immersed in the fluid. We have demonstrated this fluid-pumping effect on a gold surface patterned with silver.

**Steering Committee**

One limitation of our first fluid-immersed nanorods was that they moved in random directions and were continuously undergoing random turns because of Brownian motion. In realistic applications, of course, nanomachines will need some mechanism to steer them toward their destination.

Our first attempt to solve the steering problem relied on a magnetic field [see box on page 76]. We embedded nickel disks in the rods. These disks react to magnetic fields like tiny compasses with their north-pole to south-pole axes perpendicular to the length of the cylinders. A refrigerator magnet held a few millimeters away exerts enough torque on a cylinder to overcome Brownian motion’s tendency to turn the cylinder around at random. The only remaining force is along the length of the rod, supplied by the catalytic reaction. Our nanorods then move in straight lines and can be steered by turning the magnet. This motion is analogous to the behavior of bacteria that align themselves with the earth’s weak magnetic field. Similar motors can navigate in a microscale magnetic labyrinth, following the field lines through twists and turns.

Last year Crespi and one of us (Sen) showed that the magnetically steered motors are able to pull “cargo” containers—plastic spheres about 10 times their size—through fluids. Many interesting applications can be envisioned for such cargo-bearing motors. For example, they could deliver drugs to particular cells in the body or shuttle molecules along a nanoscale assembly line, where the cargo could chemically bind to other molecules.

Steering nanorobots externally could be useful in some applications; for others, it will be essential that nanorobots be able to move autonomously. Velegol and Sen were excited to discover recently that our catalytic nanorods can follow chemical “bread crumb trails” the way bacteria do. Typically a bacterium moves by a series of straight runs interrupted by random turns. But when a straight run happens to swim up a chemical gradient (for example, the scent of food becoming more intense closer to the food itself), the bacterium extends the length of the straight run. Because favorable runs last longer than those in unfavorable directions, the net effect is that the bacterium eventually converges on its target, even though it has no direct way to steer itself—a strategy called chemotaxis.

Our nanomotors move faster at higher con-
centrations of fuel, and this tendency effectively lengthens their straight runs. Consequently, they move on average toward a source of fuel, such as a gel particle soaked with hydrogen peroxide [see photographs on next page and video online].

More recently, the two of us have also demonstrated motor particles that are driven by light, or phototaxis. These particles use light to break up molecules and create positive and negative ions. The two types of ions diffuse away at different speeds, setting up an electric field that causes the particles to move. Depending on the nature of the ions released and the charge on the particle, the particles are driven toward or away from the region of highest light intensity. An interesting twist on this technique is a light-driven system in which some particles act as “predators” and others as “prey.” In this case, one kind of particle gives off ions that cause the second kind to be driven toward it. The correlated motion of these particles bears a striking resemblance to white blood cells chasing down a bacterium.

Chemotaxis and phototaxis are still at the proof-of-principle stage, but they could lead to the design of “smart,” autonomous nanorobots, which could move independently toward their target, perhaps by harvesting energy from glucose or other fuels abundant inside organisms or in the environment. Our work can also be a starting point for the design of new robots that could communicate chemically with one another and perform collective functions, such as moving in swarms and forming patterns.

Scaling Down

Although the particles exhibiting these collective behaviors are “inanimate,” their movement is governed by similar physical phenomena as that of living cells. Thus, nanomotors not only take inspiration from biology, they also offer insight into how the moving parts of living systems work. One of the simple rules we learned in studying catalytic nanomotors is that the typical cruise speed of a nanomotor

The authors created two-micron-long gold-platinum rods that propel themselves in a solution of water and hydrogen peroxide (H₂O₂) by pushing the fluid along their sides. The fluid’s flow is powered by two different chemical reactions occurring at the gold and platinum surfaces (insets). The uninterrupted flow enables the rods to overcome the fluid’s viscosity. Catalytic engines could help bacterium-sized robots navigate inside the human body, and can drive microscopic machine parts such as gears (micrograph at far right).

1 PROTONS NEEDED
The gold surface catalyzes a reaction that takes protons, electrons and H₂O₂ and produces H₂O. The reaction calls for protons and electrons to flow in from the platinum side.

2 PROTONS DRAG WATER
Electrons flow inside the rod, and equal numbers of protons slide along the rod’s surface. The protons’ positive charges attract water molecules, which get dragged along.

3 PROTONS PRODUCED
The platinum surface continuously generates the needed protons by catalyzing the breakdown of H₂O₂ into electrons, protons and O₂.

[HOW IT WORKS]

ANATOMY OF A CATALYTIC ENGINE

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Smallest free swimmers in all of biology. At smaller scales, Brownian motion makes it all but impossible to keep a steady direction of motion while immersed in a fluid. In fact, all molecular-scale motors in nature—including muscle proteins and the enzymes that produce ATP—are either constrained to run along a track or embedded in a membrane. The same will have to be true of any future molecular-scale robots.

**Ratcheting Up**

For molecular-scale motors, simple catalytic nanorods tend to move in random bursts in the presence of fuel, but the bursts last longer where the fuel concentration is higher. The net effect is that nanorods move up the fuel's chemical gradient much as bacterial flagella do in Brownian motion. Catalytic reaction as demonstrated in our nanorods may also be too inefficient to counter Brownian motion, whether or not the robot's motion is constrained. Nature, however, has found ways to put Brownian motion to work rather than fighting it. Many biological motors, which use energy from chemical catalysis to create motion in a certain direction, use the Brownian motion of the water molecules to work rather than against it. These motors have recently been demonstrated by Olin Velev of North Carolina State University and his collaborators. They have recently shown how to propel objects in fluids without any fuel. Their vessels contain a diode, a device that allows electric currents to cross it in one direction but not in the other. The researchers apply an alternating electric field. In the vicinity of the vessel, the diode converts the alternating field into a static one. The static field points in a constant direction, producing a net force that provides a thrust.

FREE LUNCH (AT A COST)

Molecules are never completely still. In the case of a liquid, the random movement is known as Brownian motion. Chemists are creating the first artificial Brownian ratchets, molecular-scale machines that harness Brownian motion rather than fight against it. David Leigh of the University of Edinburgh and his team, for example, are developing a monorail system that turns random steps into directed motion (below). Their invention might seem to be a perpetual motion machine, in violation of the laws of thermodynamics, or of the “no free lunch” rule. But any method of selecting Brownian motion must itself expend energy in the selection process, and this one is no exception: if the supplied energy ends, the motion stops.

1 VEHICLE MOVES RANDOMLY
A “vehicle” molecule can move in steps along a “monorail” immersed in a liquid. The engineless vehicle is subject to the fluid’s Brownian motion, so it jumps back and forth each time it’s hit by an unusually fast molecule from the liquid.

2 ROADBLOCKS COME INTO PLAY
Molecules in the liquid can also bind to the railing and act as roadblocks. But the vehicle is designed to be asymmetric, so that it prevents the roadblock molecules from binding directly in front of it.

3 RANDOM BECOMES DIRECTED
Now, when Brownian motion hits the vehicle, the roadblock behind it prevents it from backing up. The roadblocks thus increase the vehicle’s chances of moving one step forward rather than one step backward.

4 SLATE IS CLEANED
The solution periodically breaks down the blocking molecules so that the vehicle molecule can keep moving ahead. Each of its steps is random and takes energy from Brownian motion. But breaking down the roadblocks costs energy, as required by the second law of thermodynamics.

that on the centimeter to millimeter scale the speed of a diode motor does not vary with its size, in agreement with theory. That result implies that such motors could be quite powerful on the scale of tens of microns, which is about the size of a human cell.

Thanks to the advances of computer chip technology, it is now possible to make diodes well below the scale of microns, and molecular diodes only two to three nanometers in length have long been synthesized chemically. It may thus become possible to make microscopic scalpels that consist of propulsion, steering and sensing components patterned onto tiny silicon chips. One can imagine driving diode-powered scalpels wirelessly and remotely with radio-frequency electric fields, which are not absorbed by the body. Ultimately, these microscalpels might be delivered with a very fine needle and piloted to their destination by remote control.

Scientists (and science-fiction writers) have contemplated nanomachines at least since 1959, when physicist Richard Feynman considered the limits of scale for machines and information storage systems in a forward-looking lecture entitled “Plenty of Room at the Bottom.” He pointed out that the laws of physics are valid down to the length scale of molecules. There is, therefore, no reason, apart from the obvious challenges of making them, that one should be prohibited from constructing vehicles or even the factories to mass-produce nanomachines from atomically precise molecular parts.

In the intervening decades, Feynman’s lecture has continued to inspire research in nanotechnology. Meanwhile the prevailing view of the living cell has shifted from a soup pot of enzymes carrying out metabolic reactions to a ticking Swiss watch of mechanically linked nanomotors. Thus, in many ways, cells are the molecular factories that Feynman envisioned.

Investigators have learned a good deal about how to make nonbiological motors inspired by those of biology, but there is still much to learn about the principles of catalyzed movement on this length scale. No doubt future work will find as yet unimagined ways to exploit such knowledge in biomedicine, energy conversion, chemical synthesis and other fields.

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