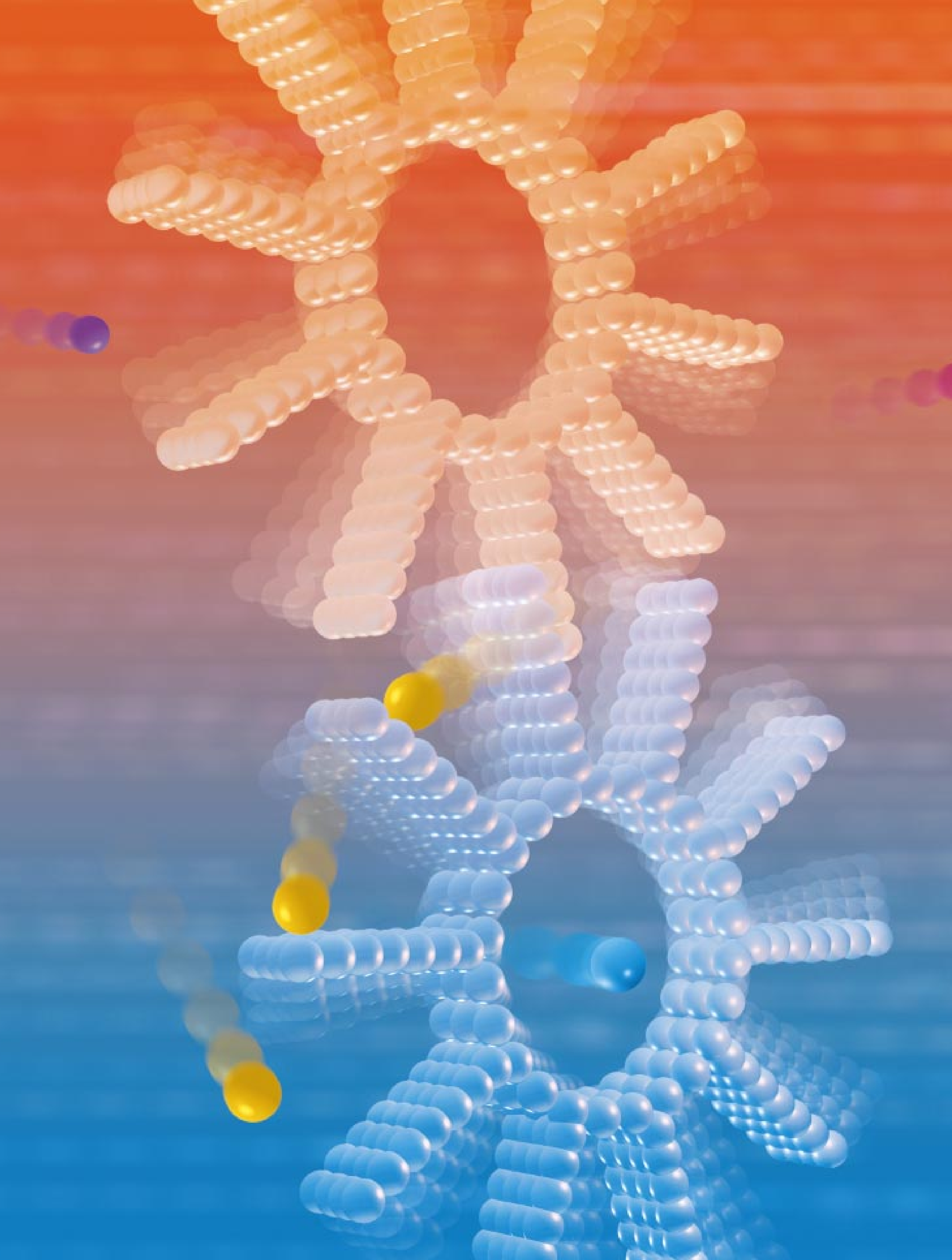


MAKING molecules INTO motors

Molecular turmoil, quantum craziness: microscopic machines must operate in a world gone mad. But if you can't beat the chaos, why not exploit it?

BY R. DEAN ASTUMIAN

HUDDLED IN THE RUINS OF a house in southwestern London, the protagonist of *The War of the Worlds* marveled at the strangeness of Martian technology:

> Of their appliances, perhaps nothing is more wonderful to a man than the curious fact that what is the dominant feature of almost all human devices in mechanism is absent—the *wheel* is absent.

An advanced technology can do away with things we regard as absolutely essential. Just that is happening now in a blossoming field at the intersection of physics, chemistry and biology: the study and construction of devices that serve as motors and pumps on the molecular scale. These mechanisms generally lack rotors, armatures and all the other trappings of conventional engines, but that is the least of their oddities. In an ordinary motor, energy is used to cause motion. In these motors, energy is used to cause a cessation of motion. Although they seem rather like an example of alien technology, they are the most common type of motor on our planet, the basis of the inner workings of all living cells.

Our physical intuition, formed by everyday observation of large machines, fails when we consider the world of the small. It is a capricious world, ruled by thermal and quantum fluctuations. For molecules, moving deterministically is like trying to walk in a hurricane: the forces propelling a particle along the desired path are puny in comparison to the random forces exerted by the environment. Yet cells thrive. They ferry materials, they pump ions, they build proteins, they move from here to there. They make order out of anarchy.

Over the past several years, researchers have finally begun to understand how. The basic insight, loosely described as the Brownian ratchet principle, is that random noise can be put to good use. The trick is to rectify the noise, to filter out the randomness you do not want so that you are left with what you do want. This principle resembles the phenomenon known as stochastic synchronization, whereby increasing the noise in a communications channel can actually make it easier to transmit a signal [see "The Benefits of Background Noise," by Frank Moss and Kurt Wiesenfeld; SCIENTIFIC AMERICAN, August 1995].

Using the techniques of chemistry, researchers have been designing miniature motors and devices that can manipulate molecules one at a time. These tiny machines imitate what protein motors and pumps do in living cells—convert chemical energy into mechanical work with almost 100 percent efficiency—and could carry out such tasks as molecular assembly, fine sifting, low-energy-consumption computation and semiconductor quality control. They may be the first step in turning the science fiction of nanotechnology, the dream of atom-by-atom control of matter, into science fact.

Braking into Motion

EVEN A FREAK HAILSTORM does not come close to the tempestuous bombardment that is routine in the molecular world, but the effects can be analogous. Usually when you park your car at the foot of a hill, turn off the engine and release the emergency brake, the car will not start climbing the hill. But imagine this scenario. Hundreds of hailstones strike the car every second, hitting all sides at random. Each one transfers a small amount of momentum to move the car a tiny distance forward or backward. On average, the momentum transferred to the car is zero, but in any time interval the car will move a little more in one direction than in the other.

You can take advantage of these random pushes in a very simple way. Put a brick behind the rear wheel to prevent the car from rolling backward and wait until a hailstone pushes it forward. If you do nothing, the car will soon roll back, but if you swiftly move the brick, you can trap the car in its new position. By continuing this process—moving the brick each time the car lurches forward—you can drive down the street, even up a hill.

It takes a keen eye and quick wit to move a brick under a heaving car in the middle of a violent hailstorm. Fortunately, the same effect can be achieved simply by replacing the standard brake with a ratchet—a device that allows motion in only one direction. A ratchet consists of a gear with asymmetric teeth and a pawl, a little arm that jams the gear and prevents it from turning backward. In a turnstile or ratchet wrench, the pawl is spring-loaded. Such a simple ratchet mechanism would keep the car moving forward. Progress would be agonizingly slow, however, because only a small fraction of the hailstones—those with enough momentum to overcome the force exerted on the ratchet by the spring—would have any effect.

A better alternative is to skew the teeth in the opposite direction and substitute the spring-loaded pawl with a piston activated by the brake pedal. When the brake is off, the piston is disengaged, and the car is free to lurch back and forth. When the driver pushes the brake pedal, the piston engages and locks the gear (and car) in place.

This modified ratchet does away with the need for careful measurement and intelligent intervention. All the driver has to do is sit in the car and pump the brake. Because of the skewed gear teeth, a few extra hailstones striking from behind are sufficient to move the car forward far enough to advance the gear by one tooth, whereas a larger number of hailstones from the front are necessary to push it backward by one tooth. This asymmetry ensures that the car moves forward even if the brake is engaged and disengaged randomly. The beauty of the system is that it requires no synchronization—none of the careful timing required in an ordinary engine.

Averaged over time, the hailstones exert no net force on the car. The vehicle acquires its forward motion from the application of the brake, which forces the piston down onto the gently sloping face of the lopsided teeth. Take away any component—the asymmetry of the ratchet teeth, the jittering caused by the hailstones or the external energy supplied by pumping the brake—and the mechanism would fail.

Needless to say, such a contrivance is quite unrealistic for a real car. A back-of-envelope calculation shows that a reasonable pumping rate could impart a velocity of no more than a kilometer per hour, about a tenth of the car's body length per second. The maximum force on the car would be one millionth the gravitational force, so at best the car could climb a very gradual slope.

But if the car is very small—say, the size of a large molecule—and immersed in water, the mechanism is much more effective [*see box on page 60*]. The mass

Overview / *Motors from Molecules*

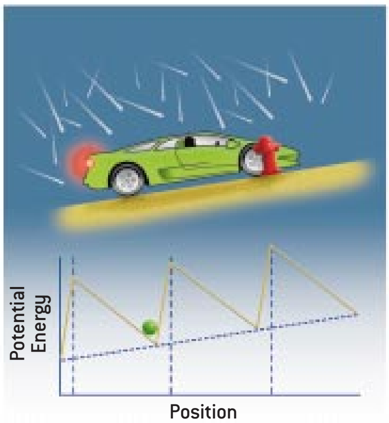
To make a molecular motor, it isn't enough just to make a miniature version of an ordinary motor. Researchers have had to rethink the very premises on which a motor operates.

- In ordinary motors, an energy input causes motion. In molecular motors, an energy input restrains motion. By selectively stopping the motions it doesn't want and letting through the ones it does—using a ratcheting mechanism akin to a ratchet wrench—the motor turns momentum from random environmental influences into organized motion.
- Ratchets sound like they get something for nothing, but the second law of thermodynamics wouldn't look kindly on that. Physicist Richard Feynman explained how these systems are completely kosher.
- Such motors make many of the dreams of nanotechnology possible. They also explain how living cells function amid the chaos of the microworld.

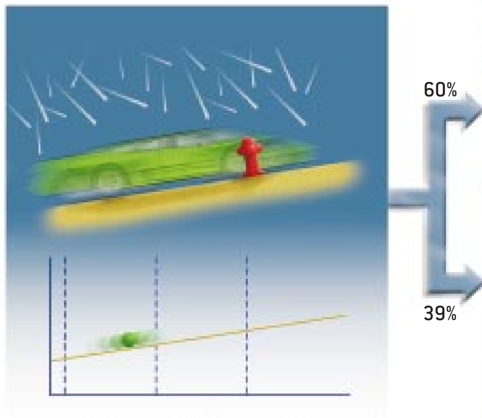
ILLUSTRATION ON PAGE 56: PHILIP HOWE

UPHILL BATTLE

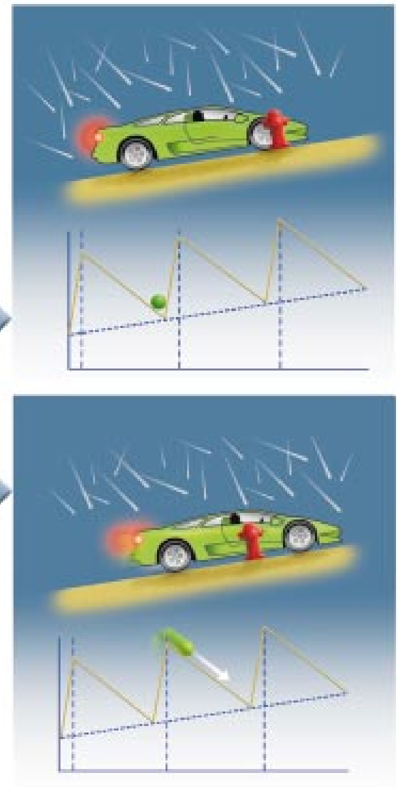
DRIVING UPHILL WITHOUT AN ENGINE is an apt metaphor for understanding molecular motors. It sounds impossible but can happen if a car is equipped with a special ratchet brake and is bombarded by hailstones. In terms of potential energy, the hill can be represented by a straight line and the brake (when applied) by a lopsided sawtooth.



When the brake is on, the car is forced down into the notch of the sawtooth. It is unlikely that a hailstone would push the car out of this locked position. (If one did, the car would actually tend to move backward—that is, the path of least resistance for the ratchet.)



When the brake is off, hailstones buffet the car, making it jiggle back and forth randomly. The probability of reaching a certain position can be calculated from the slope of the hill and the amount of time available. Despite the downhill bias, the car is more likely to move past the position of the peak to the right than the peak to the left (*dashed lines*).



Reapplying the brake pushes the car back to where it started (for this example, with 60% probability), forward one notch (39%) or back (1%; not shown).

ratio of a water molecule and a small protein is about the same as the mass ratio of a hailstone and a car. The difference is that water molecules hit the protein many billion times a second. These collisions produce the well-known jittering called Brownian motion. What is not so well known is that a Lilliputian ratchet could use Brownian motion to turn directionless energy into directed motion. A small protein could reach a velocity of one micron (more than 10 times its size) a second—the equivalent of 100 kilometers an hour for a car. The ratchet mechanism could overcome a force of up to 10 piconewtons, nearly a million times the force of gravity on a molecule.

It is amazing but true that two random processes can combine to produce a nonrandom effect. Physicist Juan M. R. Parrondo of Complutensian University in Madrid recently showed that the same principle applies to games of chance. Switching between two games, each a losing proposition, can turn the odds in your favor [*see box on page 62*].

Long Arm of the Second Law

A PHYSICIST'S FIRST reaction is that ratchets might break the second law of thermodynamics, whereby it is impossible to convert random thermal fluctuations into mechanical work. In his famous *Lectures on Physics,* Richard Feynman analyzed a ratchet attached to a paddle wheel. If the ratchet could prevent the wheel from going backward, molecular collisions would cause an irregular but relentless rotation of the wheel [*see illustration on page 61*]. The result: a perpetual-motion machine of the second kind—that is, one that defies the second law. (The device does not claim to manufacture energy out of nothing, so it does not violate the first law of thermodynamics, the law of conservation of energy.)

As Feynman showed, however, the device cannot work without an outside energy source. The pawl must be attached to the ratchet by a spring, which itself is

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PHILIP HOWE

vulnerable to thermal noise. Occasionally noise causes the spring to contract, lifting the pawl and prematurely disengaging the mechanism. Because of the asymmetry of the gear teeth, the ratchet will most likely slip back a notch. If the paddle wheel and pawl are at the same temperature, the tendencies to move forward (because of molecular collisions) and to move backward (because of the unreliable spring) exactly cancel. Despite superficial appearances, a ratchet system in thermal equilibrium will not rotate.

This restriction does not apply when the system is out of thermal equilibrium. If the paddle wheel is hotter than the spring, the ratchet rotates counterclockwise, as intuition would suggest. If the spring is hotter, the ratchet rotates clockwise—a motion that ratchets usually prevent. Any departure from equilibrium allows for ratchet-driven motion. Whatever creates the disequilibrium provides energy to the system. In the case of the car, the energy comes from the foot on the brake. The energy dissipates to heat as the car is forced into the locked position. In this way, these systems comply with the second law.

Although large thermal gradients are rare at the molecular level, other forms of disequilibrium are quite common. Three years ago organic chemist T. Ross Kelly and his colleagues at Boston College elaborated on this point with a clever experiment. They synthesized Feynman's ratchet from triptycene, a Y-shaped organic molecule that serves as the paddle wheel, and helicene, a G-shaped molecule that acts as the pawl and spring. Because the helicene has a bend in it, it is easier to turn the paddle wheel clockwise than counterclockwise. Despite this asymmetry, NMR spectroscopy showed that the frequencies of clockwise and counterclockwise turns were exactly equal, as Feynman predicted [see "Taming Maxwell's Demon," by George Musser; SCIENTIFIC AMERICAN, News and Analysis, February 1999].

Kelly's group then incorporated a nonequilibrium chemical process: the hydrolysis, or water-driven decomposition, of phosgene gas. A hydroxyalkyl group was attached to the pawl and an amino group to one vane of the paddle wheel. Together they served as a brake. Whenever the vane approached the pawl, the groups (primed by the phosgene) reacted and prevented any further counterclockwise rotation. The net effect was that most of the paddle wheels rotated clockwise. This system is not a true molecular motor—if the brake were released and reapplied, the wheel would tend to return to its starting point—but it does demonstrate the concept. Other groups have achieved continuous rotation using different ratchet mechanisms. A team headed by Ben L. Feringa of the University of Groningen, for instance, drives a molecular motor with light.

Pump the Brake

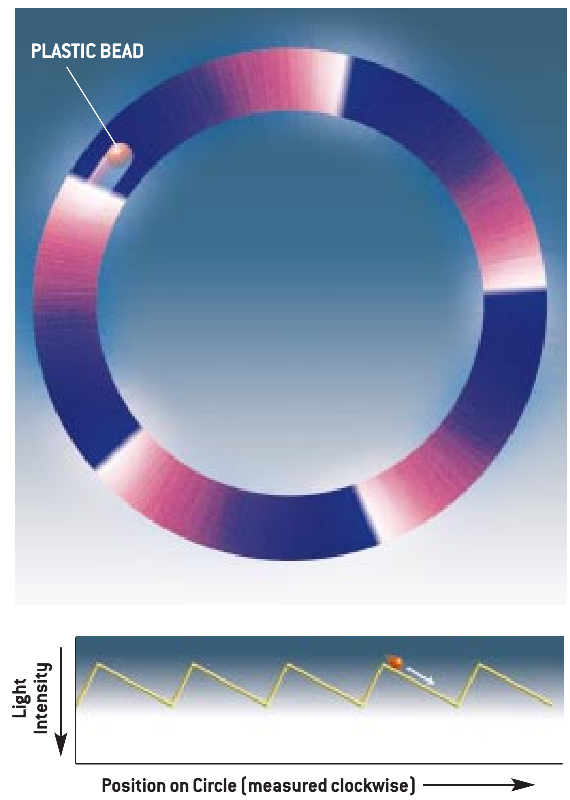
RECENT EXPERIMENTS suggest that at least some biological engines work by similar means. One example is the ion pump, a protein that pushes electrically charged particles through a cell membrane. Ions naturally flow from higher to lower

BRAKE LIGHT

BIZARRE THOUGH IT MAY SEEM, the brake-driven car is exactly analogous to a rudimentary molecular motor. In one elegant experiment seven years ago, Albert J. Libchaber, a physicist then at Princeton University, and his colleagues used a micron-size plastic bead floating in a beaker of water as the "car." They manipulated the bead using light beams; the subtle pressure of light refracted through the bead pushed it toward regions where the light intensity was strongest. One light beam created a circle of light that generally confined the bead: the "road." Superimposed on the road was a second beam that could be turned on or off: the "brake." The brake beam set up an alternating series of bright and dark regions, in which the positions of maximum and minimum intensity were not evenly spaced (*right*). Moving clockwise from a maximum, it was a short distance to the next minimum; moving counterclockwise, a long distance. This asymmetry is analogous to the skew of the gear teeth in a mechanical ratchet.

With the brake beam on, the bead moved in the direction of increasing intensity. On reaching the next maximum, it remained there as long as the brake was applied. With the brake beam off, the bead randomly lurched around the circle. If it managed to drift past a minimum, then reapplying the brake pushed it to the next maximum. Because of the asymmetry, the bead was more likely to move clockwise. The net velocity depended on how often the brake beam was turned on and off. As the frequency increased, so did the velocity, until it reached the point where Brownian motion could not keep up.

As with the car example, this system required no measurement, no choreography and no application of intelligence during operation. It worked even if the brake beam was turned on and off at random.



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Unlike an ordinary engine, a Brownian motor **REQUIRES NO MEASUREMENT** and no choreography.

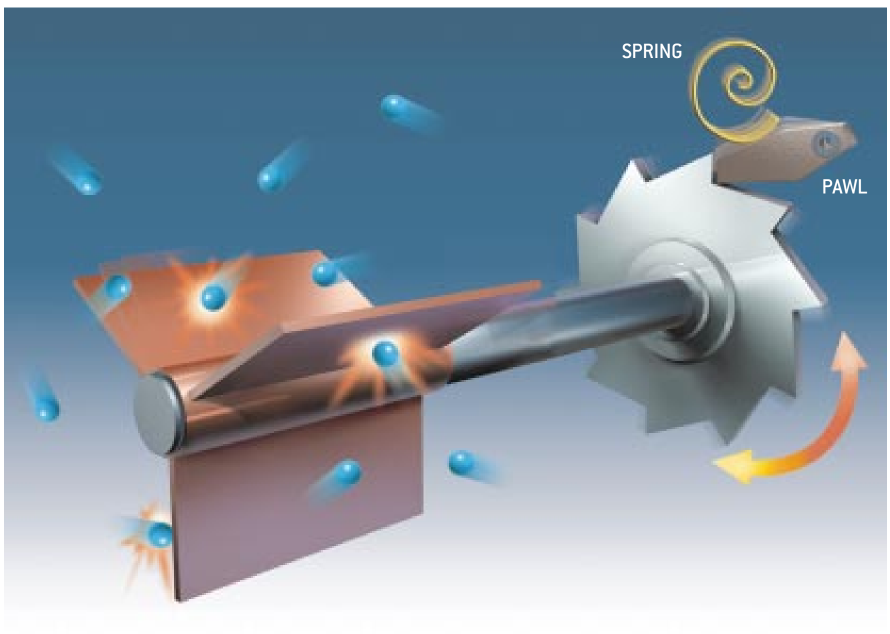
electrochemical potential, but these pumps can drive ions in the opposite direction, maintaining the electrochemical gradients essential for life.

The ion pump seems to be based on a simpler device, the ion channel. An ion channel is a biological rectifier: it allows electric current to flow in one direction only. A typical channel is a funnel-shaped protein about 10 nanometers long. Ions can move from the mouth of the funnel to the tip, but not the other way. Turning this rectifier into a pump requires some mechanism to modulate the size of the mouth and the strength of the interaction of an ion within the channel. The shape of the channel is well suited to this type of modification, because it acts like a lever: a small displacement of atoms near the tip of the funnel can result in a large change at the mouth. By making the mouth open and close cyclically, the pump can move ions from the tip of the funnel out the base—just as pumping the car brake caused the gear to turn in the opposite direction from what one would have expected.

The hydrolysis of adenosine triphosphate (ATP), the fuel used by cells, provides just the mechanism required to turn a channel into a pump. In a simplified description, the pump has two possible states. In the first state, the mouth is open to the inside of the cell and ions interact strongly with the interior of the channel. In the second, the mouth is closed to the inside and ions interact weakly with the interior. The binding of ATP favors the first state, and the release of the hydrolysis products favors the second. The process is analogous to the operation of a canal lock but with a crucial difference: it requires no control mechanism to synchronize the hydrolysis with the ion motion. It is enough to cycle randomly between two states of the protein. When the gate to the inside is open and the channel's energy level is low, an ion naturally enters the channel from the inside. When the gate to the inside is closed and the energy level is high, the ion flows to the outside. In the mid-1980s this ratchet picture was corroborated by Tian Y. Tsong, then at Johns Hopkins University, me, and our colleagues. We applied an alternating electric field to an ion pump and observed it driving ions up an electrochemical gradient, even without hydrolyzing ATP.

Another example is kinesin, a molecular forklift that transports proteins within the cell. Kinesin consists of two loosely attached domains and moves along a track called a microtubule, made of many individual molecules of the protein tubulin, each about 10 nanometers long. The electric potential between the kinesin and the microtubule usually has a sawtooth pattern, with energy barriers preventing the motion of kinesin from one tubulin molecule to the next. In the Brownian model, hydrolysis of an ATP molecule changes this potential to a flat shape and allows random collisions to jostle the kinesin. Release of the hydrolysis products returns the potential to the sawtooth shape, which, depending on how far the kinesin has drifted, can push the molecule forward.

This Brownian model of how kinesin moves differs radically from the traditional one, in which the shape of the molecule played the central role. The idea was that the two domains, acting like arms, let go of the microtubule one at a time and swing forward—as though they were moving along monkey bars in a playground. A clear prediction of this theory was that if one domain is removed, the resulting molecule should not be able to move along the microtubule. In 1998 Yasushi Okada and Nobutaka Hirokawa of the University of Tokyo replaced one of the domains with a charged loop of amino acids, so that the molecule had a different shape but nearly the same bind-



RATCHET MECHANISM studied by physicist Richard Feynman shows how random bombardment can bring about nonrandom motion. The gas molecules hitting the propeller cause the gear to turn, but which way does it go? If the spring-loaded pawl—the arm that jams the gear—works correctly, the gear can only turn counterclockwise. But when thermal noise causes the spring to release and reengage, the gear tends to turn clockwise because of the asymmetry of the gear teeth. This effect dominates whenever more heat is applied to the spring than to the gas.

PHILIP HOWE AND KEVIN RING

ing energy. This molecule moved roughly as fast as the normal two-armed kinesin, in support of the Brownian model.

Brownian motion may also play a role in the biomolecular motors that make up our muscles [*see box on page 64*], assemble our proteins, synthesize ATP, zip and unzip DNA, transport proteins across our cell membranes, and break down proteins when they are no longer needed. In some cases, the evidence is equivocal, and researchers still debate what is going on. But one thing is clear: any microscopic machine must either work with Brownian motion or fight against it, and the former seems to be the preferable choice.

The Brownian ratchet principle gives scientists and engineers a whole new way to manipulate matter on a small scale. One of the first applications has been to separate particles by weight. This process

GAMBLER'S PARADOX

THE APPARENT PARADOX of Brownian ratchets—that flip-flopping between two states of a system, each of which independently loses energy, can allow a system to gain energy—also applies to games of chance. Last year physicist Juan M. R. Parrondo of Complutensian University in Madrid and engineer Derek Abbott of the University of Adelaide in Australia came up with a pair of coin games that illustrate the paradox. If you play either game by itself, you tend to lose, but if you randomly switch between them, you tend to win. The trick is that even a losing game lets you win occasionally. By switching games, you lock in those winnings before the inevitable loss takes them away.

Although Parrondo and Abbott's game uses biased coins, other examples require only a standard (unbiased) coin and a fair (not loaded) pair of dice. For instance, consider a game that combines craps with checkers. You play it by moving a piece along part of a checkerboard. The object is to start in the middle and get to the right side before the left side [*below*]. The player moves the piece either forward or backward by rolling a pair of dice and consulting a table of craps-like rules. If the player uses either of the two sets of rules given here—which are identical except for reversing the roles of black and white—he or she tends to lose. The relative probability of winning equals the number of ways to move forward from white to black times the number of ways to move forward from black to white (8×2). Losing involves moving backward twice (5×4). For either set of rules, the player can expect only 80 wins for every 100 losses.

But suppose we allow a coin flip before each move. For heads, the player makes a move according to the first set; for tails, the player uses the second set. Now the probability of winning is the product of the average number of forward moves: $(8 + 2)/2 \times (8 + 2)/2 = 25$. The probability of losing depends on the product of the average number of backward moves: $(4 + 5)/2 \times (4 + 5)/2 = 20.25$. Thus, the player can expect to win 100 times for every 81 times he or she loses.

In this game the dice simulate thermal noise, the unfavorable odds for each game represent the overall driving force, and the coin flip acts as the random input of energy. The game has an asymmetry: according to the first set of rules, the piece tends to spend a longer number on a black square than on a white one, and vice versa for the second set of rules. The coin flip erases this asymmetry. (Sadly, the same trick will not work for two standard casino games, which lack the type of asymmetry that a simple coin toss would eliminate.)

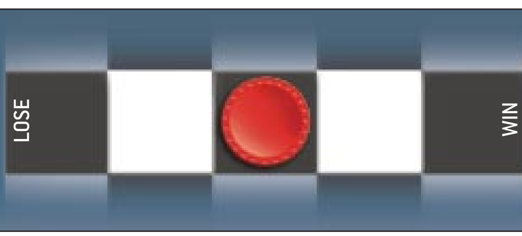
A similar reversal of fortune occurs in many areas of life; statisticians refer to it as Simpson's paradox. It can happen whenever the probabilities of some events are constant while others fluctuate. In the above example, the probability of a backward move is nearly constant while that of a forward move fluctuates depending on the outcome of the coin flip. The paradox has led researchers to draw incorrect conclusions from merged data sets and can lure the naive into subtle investment and insurance scams.

Consider a disaster insurance pool that covers both hurricanes (which tend to strike in late summer and fall) and earthquakes (which can strike year-round). In this simple example, both disasters occur at the same average rate. Floridians and Californians pay a monthly premium, and when disaster strikes, the victims receive a certain fraction of whatever money is in the fund at that time. Wily Floridians might plead that because their businesses are highly seasonal, they should pay less in the fall and winter and, to make up for it, more in the spring and summer. Would that be fair? Surprisingly, no. The Floridians' approach would make the fund larger during hurricane season, so they would tend to get larger payouts than the Californians. Using different rules, clever Californians could tilt the game in their favor. *—R.D.A.*

CRAPS-LIKE GAME involves moving a checkers piece depending on the roll of two dice. The sum on the dice determines the direction of motion. In each of the two rule sets, the piece usually moves backward, but randomly switching between the sets reverses the direction.

RULE SET 1

	WHITE	BLACK
FORWARD	7, 11	11
BACKWARD	2, 3, 12	2, 4, 12



RULE SET 2

	WHITE	BLACK
FORWARD	11	7, 11
BACKWARD	2, 4, 12	2, 3, 12

PHILIP HOWE

Using a QUANTUM RATCHET, researchers could gain precise control of individual electrons.

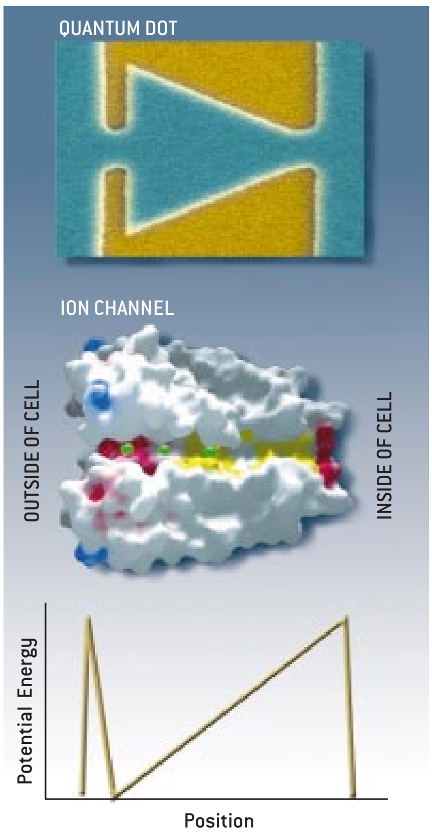
is a microscopic version of panning for gold. When you subject particles to random fluctuations—either by shaking a tray or by subjecting them to Brownian motion—the heavier ones move at a slower speed. The first steps toward building Brownian sieves were taken nine years ago by physicists Armand Ajdari of the Paris School of Industrial Physics and Chemistry and Jacques Prost of the Curie Institute. Recently Joel S. Bader and his colleagues at the biotech company Curagen in New Haven, Conn., built a device to sort DNA molecules. Their approach promises greater precision and selectivity than standard sorting techniques such as electrophoresis, centrifuge and distillation.

In all of the above ratchet examples, the ratchet electric field is either on or off. In 1996, however, Martin Bier and I (both of us then at the University of Chicago) suggested using three states: positive, negative or off. By switching among these states, a Brownian sieve could make heavy particles move one way and light particles the other way. Particles could be continuously fed into the middle of the device, collected at either end, fed into another device tuned to a different mass, and so on, with ever better separation at each stage. Such devices could sort not just by mass but also by size or electric charge. Theorists at Princeton, Chicago, the Massachusetts Institute of Technology and the University of Ottawa have since extended this idea into two dimensions.

Two years ago Alexander van Oudenaarden and Steven G. Boxer, both then at Stanford University, built a working 2-D sieve. They used electron-beam lithography to pattern a glass slide with an array of asymmetric barriers 25 nanometers high. They filled this tiny maze with a fluid of electrically neutral phospholipid molecules, mixed in some phospholipids with various electric charges and applied an electric field. The field pulled the charged molecules through the obstacle course. Because singly charged molecules moved more slowly than doubly charged ones, they had more time to drift sideways while in the space between obstacles. The asymmetric barriers made it easier for them to drift in one direction rather than simply spread out. By the time the charged molecules had reached the other side of the slide, they had sorted themselves into different groups by charge.

A Quantum Leap

IT WAS ONLY a matter of time before ratchets found their way into the quantum world. Four years ago Peter Hänggi and his colleagues at the University of Augsburg in Germany made the tantalizing suggestion that quantum effects—interference between electron wave functions, quantization of energy levels, electron tunneling through barriers—could provide another randomizing force. These effects would take over from Brownian motion at the lowest temperatures and smallest scales. Using a quantum ratchet, researchers could gain precise control of individual electrons without having to exert comparably precise manipulation of electric fields.



TWO RATCHETS differ in detail but may work in basically the same way. The micron-size triangular quantum dot, etched onto a silicon wafer, is a diode—a device that turns alternating current into direct current. The ion channel—a protein molecule shown here as a cutaway surface—is a biological version of a diode, a hundredth the size of the dot. The potential energy profile is thought to be the same for both devices.

Since that time, Charles M. Marcus, then at Stanford, and his colleagues have made an electron pump from a quantum dot, which acts as a tunnel between two larger reservoirs of electrons and can be closed off by electrostatic gates. By cycling the voltage on the dot and on the gates, Marcus's team pushed electrons between the reservoirs one by one. Because their system was always near equilibrium, the process was reversible, allowing the energy usage to be made arbitrarily small.

Two years ago Imre Derényi and I (both of us then at Chicago) designed a similar mechanism in which the voltage changes would be abrupt and random. Such a system would be intrinsically irreversible—the direction an electron is pumped does not depend on the order in which the steps are carried out—and hence more wasteful. But it would have advantages, especially as a model of irreversible chemical reactions, such as those used to drive the ion pump. Other potential applications include electron pumps in molecular computers and amplification of signals along molecule-scale wires.

Meanwhile Heiner Linke, formerly at Lund University in Sweden, and his colleagues have used triangular quantum dots. The triangles acted as ratchets because it was harder for electrons to squeeze through the vertex. When an oscillating voltage modulated this built-in bias, a net current flowed—even though the average voltage was zero. Varying the temperature

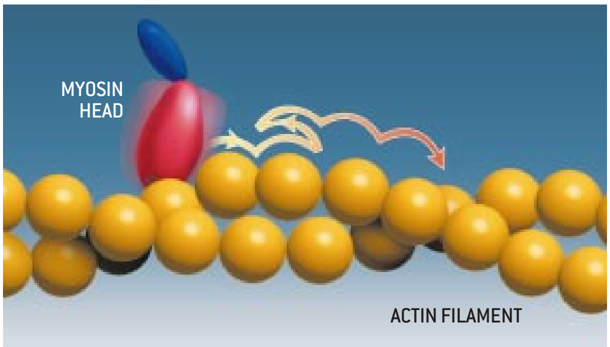
MUSCLING IN by Toshio Yanagida

ONE OF THE UNEXPECTED SUCCESSES of the theory of Brownian ratchets has been a new explanation for muscle contraction. Biomedical researchers have long known that flexing a muscle causes two kinds of filaments, made of proteins called myosin and actin, to slide along each other. The molecules convert chemical energy—in the form of adenosine triphosphate (ATP)—into kinetic energy with an efficiency of about 50 percent. This process works even if the chemical energy is barely more powerful than the noise represented by ambient heat. In contrast, artificial machines such as electric motors and car engines operate at energies much higher than the thermal noise. How can molecular motors be so efficient?

A long-held theory says that muscles contract when a molecule of myosin cleaves a molecule of ATP, gains energy and changes shape. In the process, it pulls an actin filament along by a single step—rather like climbing a ladder. This model is still popular because it posits that muscle contraction is, like the operation of ordinary motors, an easy-to-understand, deterministic process. The problem, however, is that an ordinary motor should get less, not more, efficient as it is shrunk.

To resolve this contradiction, we developed new technologies to manipulate molecules and to identify tiny movements and forces: fluorescent labeling, special short-range lighting called an evanescent field, laser trapping, and scanning probes. These efforts finally bore fruit four years ago.

We discovered that myosin and actin do not, in fact, behave deterministically. The myosin hopped stochastically in steps from 5.5 to 27.5 nanometers long. Each step was a multiple of 5.5 nanometers, equal to the separation of actin molecules in a filament. A step, no matter how long, corresponded to the consumption of a single ATP molecule. Sometimes the myosin even jumped backward rather than forward. These findings are hard to account for with the traditional model but are quite consistent with a Brownian ratchet. Although many questions remain—for example, how exactly does ATP transform the random Brownian motion into forward movement?—the basic picture explains how muscle contractions can be so efficient: rather than trying to overcome noise, they exploit it.



MOTION OF MYOSIN, crucial to the functioning of animal muscle, shows not just forward but also backward and multiple jumps—as expected if random molecular bombardment plays a major role.

PHILIP HOWE

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regulated the direction of the current. At high temperatures the device functioned as a thermal ratchet: the electrons tended to flow out of the vertex of the triangles because once through the vertex it was harder for them to go back. At low temperatures it turned into a quantum ratchet: electrons flowed out of the base of the triangles because the width of the energy barrier was smaller in that direction, thereby making tunneling faster. In addition to their applications in electronics, quantum ratchets could be used to damp the current vortices that develop in superconductors, thus resolving a major problem for magnets and superconducting wires.

These ideas bring us full circle. A century ago Brownian motion helped tremendously in demonstrating the existence of atoms. It also explained chemical reaction rates as a balance between thermal noise, which brings molecules together, and electric repulsion, which pushes them apart. The concepts filtered into biology as a possible explanation of biological transport driven by nonequilibrium chemical reactions. Nowadays biological systems are inspiring the design of chemically synthesized molecular motors and pumps, sophisticated sieves and quantum rectifiers. The flow of ideas has reversed, and the progress is anything but random. In the near future, using the principles of chemistry rather than of mechanical engineering, we may have micron-size factories assembling nanometer-size parts for motors to perform microscopic surgery; pumps to rid the factories (and maybe our cells) of unwanted waste products; and transistors for molecular computers to control these and other processes. Just as in *The War of the Worlds*, which ends with the Martians being felled by humble germs, the small may end up conquering the large. SA

MORE TO EXPLORE

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For a simulation of a basic ratchet, visit **monet.physik.unibas.ch/~elmer/bm**