Hands-on Computing: How Multi-touch Screens Work

SCIENTIFIC AMERICAN

Neuroscience and DANCING
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Prehistoric Migrations

New genetic evidence reveals clues to the first human journeys

Quantum Universe

Simple Ways to Create Spacetime

Bodyguard Proteins

Fighting Stress but also Cancer

Farming Revolution

Conserve Soil—Stop Plowing

FEATURES

SCIENTIFIC AMERICAN July 2008 ■ Volume 299 Number 1

Photoillustration by Jen Christiansen; Ryan McVay, Getty Images (*woman's face*)

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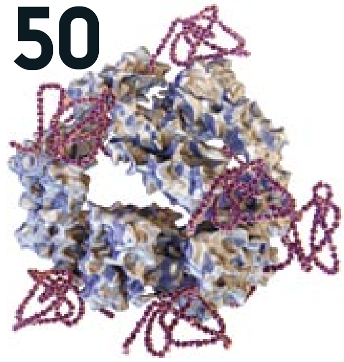

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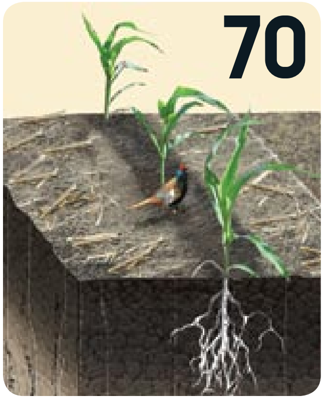

ON THE COVER

The paths that our ancestors followed out of Africa have been obliterated by time, but hints of them survive in the genetic legacies of populations spawned along the way. Image by George Retseck.

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Play the Puzzles

Get a better feel for sporadic simple groups by trying three games at **www.SciAm.com/jul2008**

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HEAD GAMES: VIDEO CONTROLLER TAPS INTO BRAIN WAVES ▼

Emotiv Systems introduces a sensor-laden headset that interprets gamers' intentions, emotions and facial expressions.
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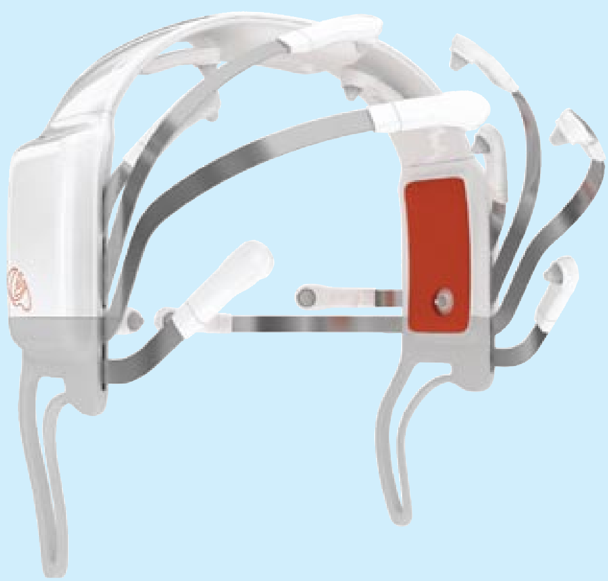

COURTESY OF EMOTIV SYSTEMS

Feature
The Origin of Menopause
New research sheds light on why women survive for decades, whereas females in many other species die after they lose the ability to reproduce.

News
Aztec Math Used Hearts and Arrows
Archaeologists discover early Mesoamerican units of measurement.

Strange but True
Identical Twins' Genes Are Not Identical
Twins may appear to be cut from the same cloth, but their genes reveal a different pattern.

Gallery
Fifty Years of American Space Exploration
NASA celebrates half a century of American spaceflight with a new collection of space exploration images.

Video
The Monitor—Fewer Rubles Meant Better Health for Cubans
Scientific American's irreverent weekly news roundup tackles Cuba's "special period."

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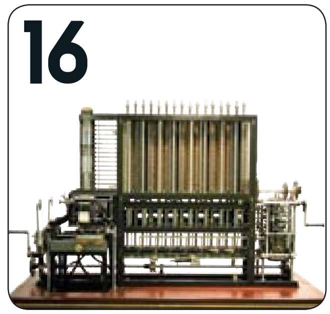
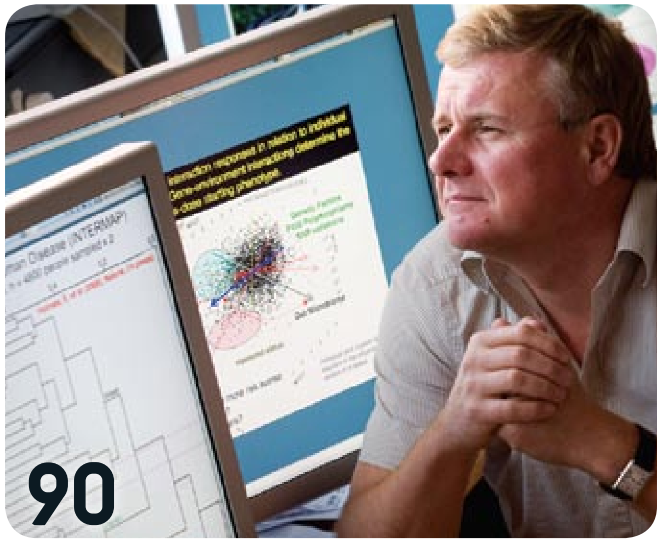
DEPARTMENTS





SION TOUHIG

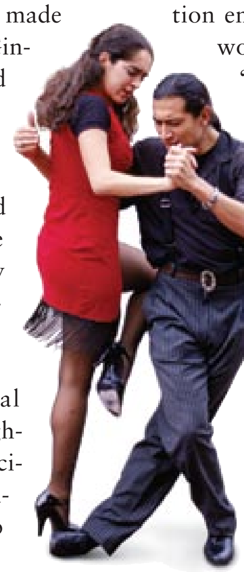
Minds in Motion

Warm up the PET scanner for a Dance Dance Brain Revolution

Never mind what's on display at the average office party or college mixer: humans have an innate ability to dance. Even toddlers spontaneously jump and sway in time to music that they like. Dance is roughly universal among the world's cultures and is often invested with great, even sacred, significance; the exceptions seem to be societies where dance was expressly forbidden because its influence was deemed too powerful.

Our terpsichorean facility appears to be an extension of our general affinity for music, which is already an evolutionary puzzle: Why do we have such advanced musical appreciation when it lacks any obvious direct survival value? But at least nature has precedents among songbirds and other creatures that respond to music. As Steven Brown and Lawrence M. Parsons note in their article about "The Neuroscience of Dance" (*page 78*), our propensity to link rhythmic movements to music is apparently unique. Humans are not merely the Fred Astaires of the animal kingdom: they are the only ones on the ballroom floor.

Always graceful, Astaire made dancing look easy (as did Ginger Rogers, who paralleled every step backward and in heels). The reality is that moving our bodies precisely, rhythmically and expressively through space while coping with gravity and balance is a highly demanding challenge. Yet even if few of us can rival the success of professional dancers at the feat, it is roughly within our natural capacities. The neural circuitry involved extends from deep within the brain stem to the cortex, as Brown and Parsons have learned by scanning the brains of dancers in the act. Read their article for details of how they peeked inside dancers' heads and be sure to look at the pictures immortalizing what is probably the first tango ever performed in a PET scanner.



TANGO through the temporal lobe.

One intriguing detail of their discoveries suggests that the right hemisphere's anatomical counterpart to one speech center becomes active during interpretive dance. Admirers of the art often talk about the "language of dance," and the scientists' work suggests that this may be more than a metaphor. Perhaps movement constituted a form of language, or at least nuanced communication, long before our ancestors ever spoke aloud. Society has been slow to accept it, but the deaf community has made a similar point for decades in its fight to have signing recognized as a legitimate language.

Surely among the clearest and most direct ways for us humans to communicate with one another are gestures. Our machines, in contrast, have been obtuse to them. One robust area of current interface research concerns helping computers to interpret gestures, and a practical application emerging from one corner of that work has been the development of "multi-touch" screens for phones and other devices. Users can shrink, enlarge, rotate or otherwise manipulate images with pinches, flips and other intuitive movements of the fingers against the screen. The beauty of the systems is that working with them is so natural—but years of hard innovation went into their development. Journalist Stuart F. Brown (no relation to Steven!) describes how these devices work, starting on page 64. ■

JOHN RENNIE
editor in chief

FLYNN LARSEN (*Rennie*); PETER MCBRIDE *Aurora Photos* (*dancers*)

Among Our Contributors

STEVEN BROWN directs the NeuroArts Lab at McMaster University in Ontario, where his research focuses on the neural basis for various types of human communication.

STUART F. BROWN writes about technology and engineering for many publications. He last wrote for *Scientific American* about display technology in the June 2007 issue.

DAVID R. HUGGINS is a soil scientist specializing in conservation cropping systems and their influence on soil quality for the USDA-Agricultural Research Service.

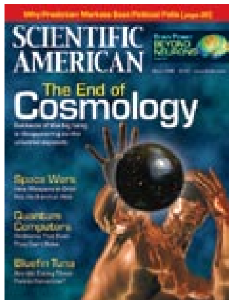
IGOR KRIZ studies algebraic topology and mathematical physics at the University of Michigan at Ann Arbor, where he is a professor of mathematics.

LAWRENCE M. PARSONS is a professor of psychology at the University of Sheffield in England who explores the mental components of dancing, singing and other musical performances.

JOHN P. REGANOLD works on sustainable agriculture at Washington State University, where he is a professor. The article in this issue is his third for *Scientific American.*

PRAMOD K. SRIVASTAVA is a professor of medicine and directs the Center for Immunotherapy of Cancer and Infectious Diseases at the University of Connecticut School of Medicine.

Schizophrenia ■ Markets vs. Polls ■ Expanding Universe



MARCH 2008

"The assertion that a market was more accurate than a poll 100 days before an election is only meaningful if one assumes that the distribution of opinion was frozen over those 100 days."
—*Jorgen Rasmussen* IOWA STATE UNIVERSITY

■ Disease of Development?

In "White Matter Matters," R. Douglas Fields reports that myelination problems are implicated in schizophrenia. Certain studies have found that the long-term outcome for schizophrenia patients is better in developing countries than in developed ones. Because myelin formation continues into one's 20s and is affected by experience, is it possible that an enriched living situation could help such patients recover some impaired myelin? Or that psychiatric drugs (less available in developing countries) blunt neuronal activity that could assist further myelination?

Phil Thompson
Los Altos, Calif.

FIELDS REPLIES: *The parallel between schizophrenia recovery rates and reliance on medication in developing and developed countries is interesting and may offer practical insights. But schizophrenia is a complex disorder that has both genetic and environmental components, making it difficult to conclude that either one's drug therapy or living situation provides a superior approach to treatment.*

Both approaches may in part affect schizophrenia via effects on myelin formation. In addition to causing myelin-forming cells to respond to altered functional activity in the brain, antipsychotics may have direct effects on oligodendrocytes. Until recently, it was not appreciated that oligodendrocytes have many of the same neurotransmitter receptors and transporters that are in neurons, including those that are implicated in schizophrenia. Antipsychotics such as haloperidol can affect the survival of oligodendrocytes.

In animal studies and postmortem analyses of schizophrenia patients, loss of oligodendrocytes is typically seen, but some studies report that dopamine protects oligodendrocytes from injury and that antipsychotic drugs boost synthesis of lipids needed to form myelin.

Most likely myelin is involved in many aspects of schizophrenia. In ignoring the role of myelinating glia in mental illness until now, researchers were playing with only half a deck. Novel treatments may come not only from recognizing treatments' ancillary effects on myelin formation but also from using the rest of that deck. Drugs might be devised to target myelinating glia specifically, offering new possibilities for this tragic disease.

■ Market Correction

In "When Markets Beat the Polls," Gary Stix details studies that suggest markets using securities for candidates "predict" the results of elections better than polls do. But polls do not make predictions; they simply report the state of opinion at a specific time. The assertion that a market was more accurate than a poll 100 days before an election is only meaningful if one assumes that the distribution of opinion was frozen over those 100 days. What method can provide the "actual" opinion 100 days in advance to serve as a comparative measure of accuracy?

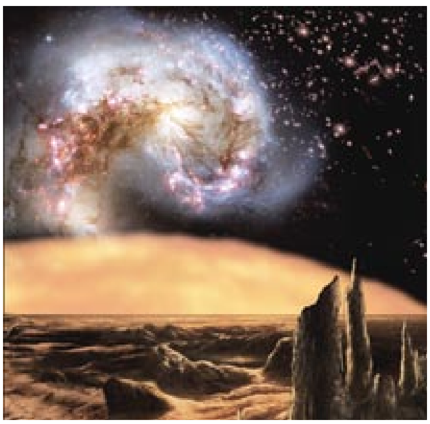
Furthermore, all polls have a sampling error. An election-day poll reporting that a candidate has 52 percent of the vote is accurate if that candidate receives anywhere from 49 to 55 percent. Markets do not have to contend with a sampling error, so they do provide more precise results, but that does not make them more accurate. A market result may be closer to what a candidate received, but if that candidate's share is within a poll's band of sampling error, the poll is just as accurate.

Jorgen Rasmussen
Distinguished Professor Emeritus
Iowa State University

Growing Up Fast

"The End of Cosmology?" by Lawrence M. Krauss and Robert J. Scherrer, states that the quickening expansion of the universe will eventually pull galaxies apart faster than light, causing them to drop out of view. It was my understanding, however, that according to relativity theory, objects cannot move faster than the speed of light relative to an observer.

Jonathan Nichols
San Francisco



DON DIXON

ALTHOUGH ACCELERATING EXPANSION will cause distant galaxies to recede from view over billions of years, the Milky Way galaxy will merge with its neighbors.

According to Krauss and Scherrer, a direct implication of the accelerating expansion of the universe they describe is that three quarters of the energy in the universe is "dark"—in other words, a mystery. I have to question whether the authors have extrapolated the consequences of accelerating expansion beyond the point where it is reasonable to be so authoritative.

Steve Didcott
Great Missenden, England

KRAUSS REPLIES: *Regarding Nichols's letter, in general relativity superluminal travel is possible, but one has to be careful about what one means. Special relativity implies that nothing can travel through space faster than light speed. General relativity, however, allows for the possibility that objects that are locally at rest in their background inertial frame can be separating from distant objects at greater than light speed because the space between these objects is expanding faster than light. There is no limit on the expansion rate of space. Even in a universe of nonaccelerating expansion (that is big enough), there will always be objects receding from one another at greater than light speed. A* Scientific American *article by Charles H. Lineweaver and Tamara M. Davis addresses the subject at www.SciAm.com/jul2008.*

As to Didcott's letter, it is true that one must be wary of extrapolations into new domains in physics. I should point out, however, that it is not simply the acceleration of the universe that implies dark energy. All the other observations in cosmology, particularly the estimates of big bang nucleosynthesis, the measurements of galaxy clustering, and the inference that the universe is flat (confirmed by observations of the cosmic microwave background), appear to be consistent only if we assume dark energy's existence. Because we do not know the nature of dark energy, we cannot say with any real certainty that the rest of the universe will disappear in the far future. But the possibility is fascinating, not least because it points out how dependent we are on our observations in framing conceptions of the cosmic past and future.

ERRATA "White Matter Matters," by R. Douglas Fields, attributes Fields's article "Myelination: An Overlooked Mechanism of Synaptic Plasticity?" to *Neuroscientist,* Vol. 11, No. 5; 2005. The article appeared in Vol. 11, No. 6 of that journal.

"When Markets Beat the Polls," by Gary Stix, incorrectly refers to John Poindexter as a previous head of the Defense Advanced Research Projects Agency (DARPA). Poindexter was the director of DARPA's former Information Awareness Office.

The photograph of microdissected tumor samples in "Solving a Massive Worker Health Puzzle," by Carole Bass, should have been credited to Sydney D. Finkelstein, chief scientific officer of RedPath Integrated Pathology, Inc.

Letters to the Editor

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Letters may be edited for length and clarity. We regret that we cannot answer all correspondence.

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Compiled by Daniel C. Schlenoff

JULY 1958

SECRECY—"A House of Representatives report concluded that 'the Federal Government has mired the American scientist in a swamp of secrecy' and that the classification of scientific information played a part in 'the nation's loss of the first lap in the race into space.' A central problem was the persistent tendency to overclassify documents. Witnesses ascribed this partly to 'the neurosis of the times' and partly to the fact that 'there is no penalty for stamping something secret which shouldn't be kept secret.' The report notes that more than a million persons now have the authority to classify information."

PRESTRESSED CONCRETE—"Concrete is made stronger by compression; steel, by tension. These opposing properties are combined to make a building material which is stronger than reinforced concrete and cheaper than steel alone. The combination is called prestressed concrete. Developed within the last few years, it is already recognized as one of the great advances in construction of the 20th century. Thousands of buildings and bridges have been built of it, and the manufacture of prestressed concrete in the U.S. is approaching a billion-dollar industry. It seems not too much to say that in construction we are passing from the age of steel to the age of prestressed concrete."

JULY 1908

CURTISS FLIES—"Aero Club of America members and others interested in aviation made the trip to Hammondsport, N.Y., to witness the flight of the Aerial Experiment Association's third aeroplane, the 'June Bug,' on the Fourth of July, for the Scientific American trophy. The distance to be covered was a kilometer in a straight line, this being the required distance for the first contest. As Mr. Curtiss was the first aviator to come forward with a practical aeroplane and request a trial, according to the rules, if he performed the flight set, he would be the first winner. The second attempt was made at 7 P.M. In this flight the machine rose quickly, and sped rapidly on at a height of some 20 feet. As it neared the finish post, it dropped to about 15 feet, and then continued onward, making a wide sweep to the left, and alighting without damage in a rather rough field. The distance traversed was easily a mile. We congratulate him at his success in winning our trophy for the first time."

SCIENTIFIC AMERICAN Aeronautic Trophy, 1908

WINNING FLIGHT of the Curtiss aeroplane for the Scientific American Trophy, July 4, 1908

➡ The entire article from 1908 is available at **www.SciAm.com/jul2008**

JULY 1858

TELEGRAPH CLAIMS—"It is well known that the English claim the invention of the magnetic telegraph for their countryman, Prof. Wheatstone. The Transatlantic telegraph enterprise has caused the subject of priority of invention to be much talked of in Europe. The Paris *Moniteur* says: 'No doubt the discovery of the principles upon which the electric telegraph system is founded does not belong to M. Morse, but he was the first to transfer that discovery from the region of speculative science into that of practical application.' "

TOAD TRAP—"An Illinois correspondent gives an account of a new insect trap that will no doubt be very successful. He says—'Procure a large toad, such as St. Patrick banished from Ireland (good luck to him), which are easily tamed, then make a small box with a hole near the bottom, so that the toad can put his head out. Drop some molasses on his back and put him in the box; his tongue is three inches long, and he can catch any insect that comes within his reach. This trap is not handsome but useful.' The inventor thinks it especially applicable for catching fleas, but if we should chance to have a flea for a bedfellow, we should certainly prefer his company to that of a toad alongside in a box."

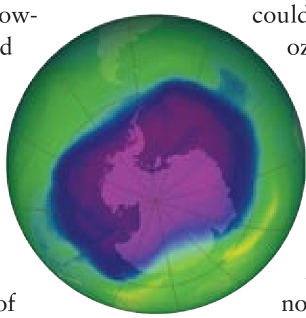
SCIENTIFIC AMERICAN, VOL. XCIX, NO. 2; JULY 11, 1908 *(top)*; *SCIENTIFIC AMERICAN*, VOL. XCIX, NO. 3; JULY 18, 1908 *(bottom)*

Ozone Warming ▪ Antiradiation ▪ Quantum Novelty ▪ Babbage Computer

Edited by Philip Yam

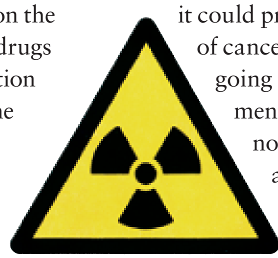
Ozone Recovery, Warmer Antarctica

The Antarctic ozone hole that forms every spring has kept that continent's interior cold even as the rest of the world has warmed over the past few decades [see "A Push from Above"; SciAm, August 2002]. Thanks to the global ban on chlorofluorocarbons, stratospheric ozone levels there are slowly recovering. A repaired hole, however, could speed Antarctic ice melting and change weather patterns, according to a computer model by Judith Perlwitz of the University of Colorado at Boulder and her colleagues. With more ozone, the lower stratosphere would absorb more ultraviolet light and warm up by as much as nine degrees Celsius. That in turn would break down circulation patterns that trap cold air over Antarctica's interior, making the continent heat up. The changed patterns would also make Australia warmer and drier, and South America could get wetter. Such ozone details may need to be worked into global climate models, most of which have neither incorporated such effects nor included enough of the stratosphere. The journal *Geophysical Research Letters* published the study on April 26.



OZONE HOLE (*purple*) has kept Antarctica cold.

Protecting Cells from Radiation



Scientists remain on the lookout for novel drugs that combat radiation damage. One of the most promising is CBLB502, made by Cleveland Biolabs in Buffalo, N.Y. [see "Surviving Side Effects"; SciAm, October 2007]. In the April 11 *Science*, researchers report that the drug, also called Protectan, enabled 87 percent of mice to survive lethal doses of radiation, although it worked only if injected within an hour before exposure. (It showed some protective effects if injected after exposure to lower levels of radiation.) The compound, which could be given in the event of a nuclear explosion or meltdown, did not shield malignant cells, so it could protect healthy cells of cancer patients undergoing radiation treatment. The company now needs to test the agent in large numbers of people.

—David Biello

Quantum Side Step

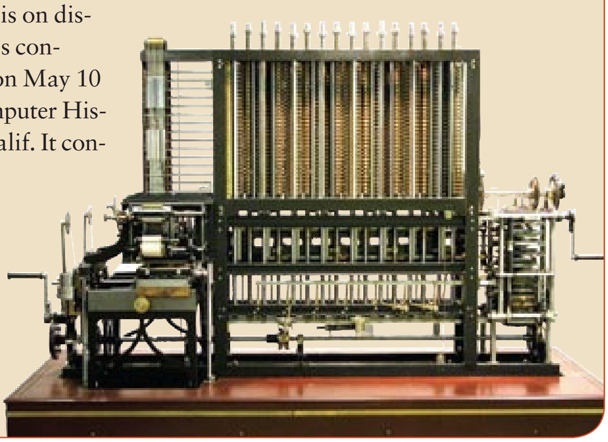
In 1879 Edwin Hall discovered that a magnet can deflect the flow of electrons, like wind pushing ships off course. In 1980 physicists observed the quantum version, in which the applied magnetic field pushes electrons in discrete steps; it is as if the ships were responding to separate gusts even though a steady wind was blowing [see "Electrons in Flatland"; SciAm, March 1996].

Now Princeton University physicists have demonstrated the quantum Hall effect without any applied magnetic field. They created special conditions for electrons in a bismuth crystal such that when the electrons travel close to the speed of light, they effectively generate their own magnetic field that deflects them. Such unusual materials not only elucidate the fundamental nature of the quantum Hall effect—it is deeply connected to superconductivity—but also could lead to novel electronic technology. The work appears in the April 24 *Nature*.

Difference Engine No. 2—No. 2

Nineteenth-century British mathematician and engineer Charles Babbage has a host of inventions to his name, including the standard railroad gauge, the cowcatcher and the ophthalmoscope. A famous design he never built is his Difference Engine No. 2, a piece of Victorian technology meant to tussle with logarithms and trigonometry. Working from Babbage's 1849 plans, Doron D. Swade, a curator at London's Science Museum, constructed the first working version of it in 1991 [see "Redeeming Charles Babbage's Mechanical Computer"; SciAm, February 1993], which is on display at the museum. Now Swade has constructed a second engine, unveiled on May 10 for a one-year exhibition at the Computer History Museum in Mountain View, Calif. It consists of 8,000 bronze, cast-iron and steel parts, weighs five tons and measures 11 feet (3.4 meters) long and seven feet (2.1 meters) high.

—Larry Greenemeier



BROUGHT TO LIFE: Charles Babbage's invention at the Computer History Museum in Mountain View, Calif.

NASA (*ozone hole*); DORLING KINDERSLEY Getty Images (*biohazard symbol*); COURTESY OF DORON D. SWADE (*mechanical computer*)

CLIMATE CHANGE

Polar Express

Ice is melting at the poles much faster than climate models predict BY PETER BROWN

The accelerating pace of climate warming in the earth's polar regions is spurring a new sense of scientific urgency. This past February 28 a camera onboard the NASA satellite Aqua caught a Manhattan-size floating piece of ice shelf in the act of disintegrating. Slabs continued to calve and break up throughout the next 10 days; by March 8 the Wilkins ice shelf, comprising some 5,000 square miles of floating ice off the coast of the Antarctic Peninsula, had lost 160 square miles of ice to the Pacific Ocean.

SHATTERED FRAGMENTS OF ICE are all that remain of a 160-square-mile area of Antarctica's Wilkins ice shelf—dramatic evidence of climate warming around the Antarctic Peninsula.

JIM ELLIOT *British Antarctic Survey*

The breakup is the latest of seven major Antarctic ice-shelf collapses in the past 30 years, after some 400 years of relative stability. They include the detachment of a 1,300-square-mile chunk from the Larsen B ice shelf, the disintegration of giant ice shelves in the Prince Gustav Channel and the Larsen Inlet, and the disappearance of ice shelves known as Jones, Larsen A, Muller and Wordie. All of them corroborate temperature measurements showing that the western Antarctic Peninsula—now known to insiders as the Banana Belt—is warming up faster than anyplace else on earth.

The Wilkins event—serendipitously caught on video by a team from the British Antarctic Survey just days after it was discovered—has rallied scientists around the world. "You have closer communication than ever among the global science community now," says Robin E. Bell, a polar research scientist at the Lamont-Doherty Earth Observatory of Columbia University. "We're more sensitive that change is really happening quickly." Relatively warm air seems to be the main culprit. As ice melts in the austral summer, pools of water fill the cracks that inevitably develop in any floating ice shelf as a result of bending and squeezing by the surrounding ocean. In a colder climate those fractures would be nothing more than shallow surface scars. But liquid water in the cracks can drill like a hot knife to the base of an ice shelf, snapping it in two.

The breakup and melting of floating ice has no direct effect on global sea levels. But an ice shelf is thought to act as a "cork in the bottle," damming the flow of the land-based glacier that slowly feeds the shelf in the sea. When such a "cork" is removed, the glacier lurches forward. "Within a few months" of a breakup, explains glaciologist Ted Scambos of the National Snow and Ice Data Center at the University of Colorado at Boulder, the glacier "accelerates significantly, and within a year or two, it can be moving [toward the ocean] up to four times as fast as it moved when the ice shelf was intact." As Bell puts it, the result is that "more ice cubes get into the ocean," which *does* raise sea level.

In the near term, however, the biggest concerns are the changes in the north: the declines of Arctic sea ice and the Greenland ice sheet. Warm air and surface water are melting the summer polar ice cap. The shrinking sea ice drives a classic positive feedback loop: as more ice melts, fewer patches of white snow reflect solar energy, and larger regions of dark, sunlight-absorbing seawater open up—both causing the ice to melt even faster. That runaway effect, Scambos says, could quickly lead to a warmer climate along the Arctic perimeter and to the loss of Arctic permafrost.

In Greenland the story of not so glacial changes in the outlet glaciers is much the same. Their seaward edges are speeding up, and the ice sheet behind them is thinning. Measurements of local gravitational anomalies by the GRACE satellites show that the Greenland ice sheet, particularly in its southern reaches, is rapidly losing mass. "The ice sheet is on a diet," Bell says. A lot of Greenland ice is slipping into the Atlantic Ocean.

Do all those effects add up to a tipping point? No one really knows. Investigators are anxiously seeking the answers to two great unknowns about the changes in polar ice. How fast will the ice sheets continue to slide into the sea, and how much more warming will it take to melt the Arctic permafrost? If the permafrost melts, prodigious amounts of trapped methane gas will burp out of the once frozen ground. Twenty years after such a release, methane is 72 times more potent than carbon dioxide (CO_2) as a greenhouse gas (after 100 years it remains 25 times more potent than CO_2), so if the methane is released, the planet risks a runaway climate catastrophe.

American Deserts from Melting Ice

The increased rate of Arctic melting could spell trouble for temperate-zone lands. Models predict that if the sea ice disappears by late summer, bands of desert will migrate northward, bringing even drier conditions than at present into the American Southwest, southeastern Europe and the Middle East. According to a study published last year by Julienne Stroeve of the National Snow and Ice Data Center and her colleagues, Arctic sea ice has declined far faster in the past 15 years than models still in use are predicting. Hence, the desertification of midlatitudes may occur before 2050—20 to 40 years sooner than predicted.

MICROBIOLOGY

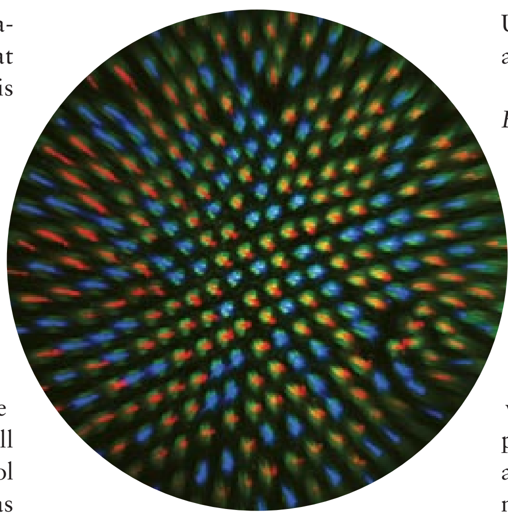
Bring In the Noise

New studies reveal how cells exploit biochemical randomness BY MELINDA WENNER

Just as identical twins raised in the same home often grow up to be different, identical cells grown in the same environment frequently exhibit distinct characteristics. These differences are the result of random fluctuations in biochemical reactions. Biologists had always thought of such biochemical blips as liabilities, but recent studies suggest that cells and bacteria sometimes utilize this randomness to their benefit.

Small systems such as cells are inherently sensitive to the random effects scientists call stochasticity—or noise—because they contain only a few active copies of individual proteins or nucleic acids. Minor fluctuations in the levels of some cellular components, for example, affect whether a particular gene turns on and makes a protein. Such noise seems to suggest that some aspects of cell fate are left to chance; the lack of control forces cells to evolve backup plans, such as redundant biochemical pathways.

Until recently, scientists had trouble studying the phenomenon, because doing so requires the ability to visualize individual cells and molecules; averaging the behavior of groups of cells cancels out noise's effects, much as fabric viewed from a distance looks flawless. In the past decade, however, a handful of new tools, including fluorescent markers that bind to molecules and light up under microscopes, have given scientists the ability to see noise in action.



RANDOM SIGHTING: **Photoreceptor cells in the fruit fly retina have been stained with various colors. Cells with red or blue respond to different hues of light. Developmental randomness ensures that these distinct cell types are distributed throughout the retina.**

CLAUDE DESPLAN *New York University*

What researchers are finding is surprising: cells sometimes appear to use noise to help them survive in changing environments and make decisions during development. "Normally, living things have to cope with noise, but sometimes they exploit it," says Richard Losick, a biologist at Harvard University, who in April co-authored an article on stochasticity in *Science*.

For example, one fifth of bacteria in *Bacillus subtilis* colonies live in a specialized state called competence, in which they stop growing and incorporate DNA from the environment into their genomes. Whether a cell enters this state is determined stochastically, and despite its costs—competent cells do not grow and divide—competence is thought to provide an evolutionary advantage in that it allows a colony to expand its genetic toolbox. Competent cells are most likely "on the prowl for new genetic sequences that could improve their fitness for changed circumstances in the future," Losick remarks.

More complex organisms also use noise to their advantage. The eye of the common fruit fly, *Drosophila melanogaster*, comprises smaller units, each consisting of eight cells. When each cell develops, it makes a choice determined by the presence or absence of a regulatory protein. This protein becomes active only in a random subset of the cells, and its occurrence determines whether the cell will respond to a particular hue of ultraviolet light. Random expression of this regulatory protein ensures that the two cell types are apportioned throughout the eye by chance so as to avoid repetitive patterns that could limit the fly's overall vision. Even though the cells "are in an identical environment and they all come from an identical ancestor, they acquire different phenotypes," or physical traits, says Mads Kaern, a systems biologist at the University of Ottawa.

Although noise plays an important role in a cell's fate, much remains to be learned about the sources of this noise and the extent to which it affects cells and other organisms, including humans. "We know a few [mechanisms], but there's a lot of evidence that there are tons more," notes Edo Kussell, a biophysicist at New York University. Another difficult task will be deciphering their biological relevance. For instance, speculating why bacteria become competent is easy, but proving that speculation is next to impossible. "Can we find a way to demonstrate that a particular stochastic mechanism has really been tuned to evolution? How do we conclusively demonstrate that?" Kussell asks.

As scientists focus on the behavior of individual cells and molecules, another problem arises, too: it becomes difficult to observe processes without affecting them. "We have to do something with the cell in order to analyze it, and we don't really know how those manipulations affect it," Kaern says.

Understanding noise will therefore involve overcoming a number of technological hurdles, but no one doubts that the endeavor is worth the undertaking. Noise could have important implications for many fields, including medicine: if cells and bacteria make a number of their decisions stochastically, then scientists might need to understand noise to develop new antibiotics and to optimize cell-based treatments such as stem cell therapy. "We need to understand how noise works within a network context; how it's used by organisms," Kaern says. "It's a very exciting field—but a little bewildering sometimes."

Melinda Wenner is a freelance writer based in New York City.

ENERGY

Roping the Sun

Shrugging off massive costs, Japan pursues space-based solar arrays BY TIM HORNYAK

KAKUDA, JAPAN—In a recent spin-off of the classic Japanese animated series *Mobile Suit Gundam,* the depletion of fossil fuels has forced humanity to turn to space-based solar power generation as global conflicts rage over energy shortages. The sci-fi saga is set in the year 2307, but even now real Japanese scientists are working on the hardware needed to realize orbital generators as a form of clean, renewable energy, with plans to complete a prototype in about 20 years.

The concept of solar panels beaming down energy from space has long been pondered—and long been dismissed as too costly and impractical. But in Japan the seemingly far-fetched scheme has received renewed attention amid the current global energy crisis and concerns about the environment. Last year researchers at the Institute for Laser Technology in Osaka produced up to 180 watts of laser power from sunlight. In February scientists in Hokkaido began ground tests of a power transmission system designed to send energy in microwave form to Earth.

The laser and microwave research projects are two halves of a bold plan for a space solar power system (SSPS) under the aegis of Japan's space agency, the Japan Aerospace Exploration Agency (JAXA). Specifically, by 2030 the agency aims to put into geostationary orbit a solar-power generator that will transmit one gigawatt of energy to Earth, equivalent to the output of a large nuclear power plant. The energy would be sent to the surface in microwave or laser form, where it would be converted into electricity for commercial power grids or stored in the form of hydrogen.

"We're doing this research for commonsense reasons—as a potential solution to the challenges posed by the exhaustion of fossil fuels and global warming," says Hiroaki Suzuki of JAXA's Advanced Mission Research Center, one of about 180 scientists at major Japanese research institutes working on the scheme. JAXA says its potential advantages are straightforward: in space, solar irradiance is five to

For the U.S., Energy Security in Orbit?

U.S. interest in the concept of orbiting power stations has waxed and waned since it was introduced decades ago. NASA began studying space-based solar power after the mid-1970s oil crisis but axed its research program in 2001. The recent spike in energy prices, though, has rekindled interest. In a feasibility study released last October, the U.S. National Security Space Office urged that the U.S. immediately develop space solar power systems. It noted that "a single kilometer-wide band of geosynchronous Earth orbit experiences enough solar flux in one year to nearly equal the amount of energy contained within all known recoverable conventional oil reserves on Earth today."

CATCHING SOME RAYS: In studying how solar energy could be beamed to Earth via laser light, Hiroaki Suzuki of the Japan Aerospace Exploration Agency peers through the opening of a laser receiving station at the Kakuda Space Center in Miyagi, Japan.

TIM HORNYAK

10 times as strong as on the ground, so generation is more efficient; solar energy could be collected 24 hours a day; and weather would not pose a problem. The system would also be clean, generating no pollution or waste, and safe. The intensity of energy reaching Earth's surface might be about five kilowatts per square meter—about five times that of the sun at noon on a clear summer day at midlatitudes. Although the scientists say this amount will not harm the human body, the receiving area would nonetheless be cordoned off and situated at sea.

At a facility in Miyagi, Suzuki and JAXA researchers are testing an 800-watt optical-fiber laser that fires at a receiving station 500 meters away. A mirror reflecting only 1,064-nanometer-wavelength light directs it into an experimental solar panel. (He chose that frequency of light because it easily cuts through Earth's atmosphere, losing no more than 10 percent of its pop.) A key task will be finding a material that can convert sunlight into laser light efficiently. A leading candidate is an yttrium-aluminum-garnet ceramic material containing neodymium and chromium.

The basic science is only part of the challenge. Testing both the microwave and laser systems will require gargantuan structures in space: thin-film condenser mirrors, solar panels and a microwave transmitter stretching for kilometers and weighing 10,000 metric tons, as well as a 100-unit laser array of 5,000 metric tons that would be 10 kilometers long. The ground-based microwave antenna would have to be two kilometers long.

The total project cost would be enormous—perhaps in the tens of billions of dollars—but Suzuki and his colleagues say they are not considering the price tag. "We can't know whether this is feasible or not if we don't have the basic technology first," he says. "We're aiming to produce stable, cheap power and hydrogen at a target price of 6.5 cents per kilowatt-hour." That would be in line with conventional power generation costs of today and might make it more economically attractive.

Given current technology, transporting large-scale structures into space may be feasible only through the cooperation of space agencies on different continents. Suzuki, though, says countries in the space race are trying to develop their technologies independently while the potential militarization of space grows. "If JAXA, NASA and the European Space Agency can work together, it would be best," he adds. It all sounds like the prelude to a sci-fi saga.

Tim Hornyak is based in Tokyo.

GENETICS

Ancient Gene, New Tricks

Resurrected "jumping gene" could deliver DNA BY CHRISTINE SOARES

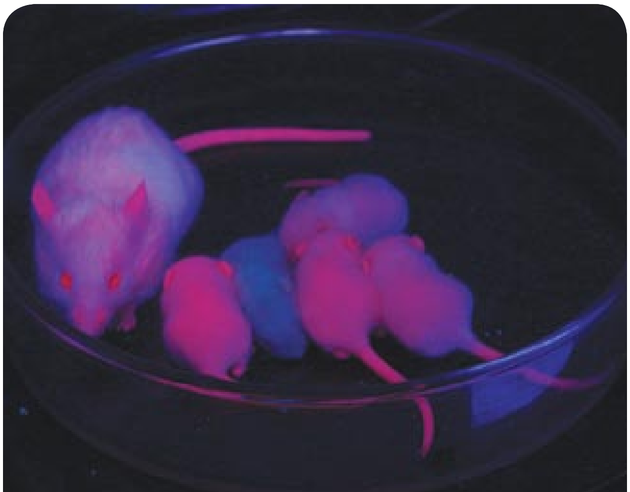
If humans could reanimate one of our ancient ancestors, we could quickly learn much more about how people once went about their lives than any study of dusty bones and artifacts would reveal. Our forebear might even teach us a few old tricks that could be used to help the living.

That is in essence what researchers in Germany and Hungary were after when they re-created *Harbinger3_DR*, a long-extinct precursor of at least two modern human genes: they wanted to watch it operate inside living cells. Not just any DNA relic, *Harbinger3_DR* is an ancient transposon—a so-called jumping gene, able to cut itself out of an organism's genome and reinsert itself in a different location. Modern scientists would love to master its secrets so they could more precisely control where genes introduced for gene therapy incorporate themselves into a patient's DNA strand.

Only vestiges remain of the original *Harbinger3_DR* in human genomes, but versions of the transposon are alive and well in other organisms, including the zebra fish. Those have shown that the gene tends to home in on genome regions containing a particular sequence of DNA. "The reason we chose *Harbinger3_DR* was this unexpectedly specific insertion site," says Zoltán Ivics of the Max Delbrück Center for Molecular Medicine in Berlin, who led the experiments. "We were hoping to use this [reincarnated] element for later studies, to understand how it selects this specific target site."

With the zebra fish gene as a template, Ivics's group synthesized a *Harbinger3_DR* with the necessary components to function in human cells. Whereas most genes encode a protein useful to the organism, transposons are self-serving parasites and encode only enough machinery to keep moving themselves around the genome. That equipment usually includes an enzyme, known as a transposase, that performs the cutting and pasting. The *Harbinger3_DR* sequence also encoded a mysterious molecule the researchers called Myb-like, for its resemblance to another protein.

The scientists delivered the construct into cultured human cells, which started manufacturing the transposons' encoded proteins. Ivics and his colleagues observed that the Myb-like protein was essential to getting the transposase enzyme into the cell nucleus and to recruiting it to the transposon's tips, where the enzyme first cuts the gene from a DNA strand and then pastes it in a new location. In follow-up experiments, Ivics wants to glean more detail about how the two proteins control the gene's insertion site. "We're hoping that we may discover aspects of the DNA interaction that can help us to specify or engineer certain domains to target a gene," he explains.



VERSATILE VECTOR: Transposons are already the preferred tool for inserting new genes into research animals, such as these mice carrying a fluorescent protein gene.

FROM "EFFICIENT TRANSPOSITION OF THE PIGGYBAC (PB) TRANSPOSON IN MAMMALIAN CELLS AND MICE," BY SHENG DING ET AL., IN *CELL*, VOL. 122; 2005, WITH PERMISSION FROM ELSEVIER

Ivics and other researchers want to press transposons into service as safer delivery vehicles for therapeutic genes. Inactivated viruses are currently the only means of permanently inserting a new gene into a patient's DNA, but the viruses integrate fairly randomly into the host genome. Viral insertion into critical genes has triggered lethal leukemias in several gene therapy recipients. Rarely, viruses can also regain their ability to reproduce, posing a risk of becoming infectious.

The keys to controlling transposons to deliver gene therapy will be learning to target them to specific areas of the genome, away from important genes, and disabling the element's jumping ability once it has landed in the desired spot, according to Margy Lambert, a molecular biologist and biosafety specialist at the University of Wisconsin–Madison. If those kinks can be worked out, Lambert says, gene delivery by transposons would represent "a major advance, because they have the flexibility to maximize the advantages [of viral vectors] and minimize the disadvantages."

Several researchers are already working on creating transposons lacking the capacity to make their own transposase. These versions could be delivered into cells with just enough of the enzyme to integrate themselves once and then stay put.

And Ivics, who in 1997 reanimated another ancient transposon that he dubbed *Sleeping Beauty,* showed last year that he could control its insertion site by directing

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it to specific target sequences. "Even if this technology is not mature enough yet for clinical use, the proof of concept has been done," he says. Studying how the *Harbinger3_DR* transposon naturally targets specific sequences may also reveal some useful new techniques.

The cooperation between transposase and the Myb-like protein is "really unusual," says Tian Xu, a geneticist at the Yale School of Medicine who works with a different transposon, called piggyBac, in mice and in human cells: "This very important study sheds new light on how transposons work."

Ivics expects the better studied of his progeny, *Sleeping Beauty*, to be ready in about five years to make her debut in a gene therapy trial.

Assimilated Genes

Transposons are the parasites of the genome: they are DNA segments that jump around to different positions, sometimes within active genes, thereby destabilizing them. Organisms have evolved mechanisms to restrain most transposons, often eliminating all but nonfunctional traces of them. The resurrected *Harbinger* transposon encodes two proteins, one of which helps the other to enter the cell nucleus and to cut and paste the jumping gene's DNA. Their interaction offers clues to similar cooperative behavior by two related human proteins, HARBI1 and NAIF1. Both are made by genes containing fragments of the ancient *Harbinger* sequence.

Zoltán Ivics of the Max Delbrück Center for Molecular Medicine in Berlin hopes that his techniques for reanimating transposons can provide tools for studying how jumping genes that lose some essential part of their jumping machinery can settle down and evolve a role within a host's genome. For instance, a human gene called *RAG-1*, also descended from a transposon, encodes an enzyme that helps immune cells respond to new pathogens by rearranging segments of their own DNA. "There are maybe a handful of examples where transposon-derived genes are described to some extent, but certainly not a lot is known about them," Ivics explains, "so it's an exciting time."

CONSERVATION

Saving Kermit

A repopulation plan for endangered amphibians BY CHARLES Q. CHOI

Amphibians are going extinct faster than any other group of organisms. Since 1980, 122 species may have disappeared. Of the roughly 6,000 remaining, up to half are threatened; some 500 could go extinct in the next 50 years if not taken into captivity. Now zoos and other institutions worldwide are working together on an "Amphibian Ark" to help save all these species as they vanish in the wild, in the hope of one day returning them home.

Amphibians may be especially vulnerable to extinction because they depend on both land and water—if either habitat suffers, they do as well. In addition, although their thin skins let them easily take in air and water, that thinness unfortunately allows pollutants through, too.

ALL ABOARD: **Giant Lake Titicaca frog and others in peril might be saved by the Amphibian Ark.**

PETER OXFORD *Nature Picture Library*

The most immediate threat to amphibians is a parasitic fungus called amphibian chytrid, which was likely accidentally spread by African clawed frogs shipped worldwide for lab studies and pregnancy tests before the 1950s. (Injecting a pregnant woman's urine into a female frog makes it lay eggs.) Once chytrid finds a suitable area, it can kill half the amphibian species there within three months, and currently scientists have no way to stop or eradicate the fungus in the wild.

Still, the greatest threat to amphibians overall is damage to or loss of habitat. For instance, one critical breeding pond of the Puerto Rican crested toad "is now a parking lot by the beach," says Jennifer B. Pramuk, curator of herpetology (amphibians and reptiles) at New York City's Bronx Zoo. Although cases of species raised in captivity and reintroduced into the wild have been documented, the sheer scope of an endeavor targeting an entire group of animals "is unprecedented," Pramuk says.

Right now zoos around the world are at best equipped to support only about 50 species long-term. The Amphibian Ark hopes to recruit 500 zoos, aquariums, botanical gardens, universities and other institutions to each support a species. For example, the Bronx Zoo and Ohio's Toledo Zoo are now helping save the penny-size, bright yellow Kihansi spray toad, which usually depends on the fine mist from the cascading waters of Kihansi Gorge in Tanzania. Its habitat withered after the Kihansi River was dammed in 2000, and then chytrid arrived; the toad has not been seen in the wild since 2003.

To keep an amphibian species breeding in captivity, about 50 wild specimens are needed for genetic diversity, estimates Kevin Zippel, the Ark's program director. "You could do it in a small room," he adds. "For the price to keep a single elephant in captivity for a year, about $100,000, you could pay for the expertise and facilities to save an entire amphibian species." Zoos and conservationists worldwide marked

2008 as the "Year of the Frog" in hopes of raising both awareness and funding, which has proved difficult to come by since the project was first proposed in 2006.

Even if saved by the project, a species might not be able to return home. The original habitat may be lost or contaminated with chytrid, which lasts for an unknown time even after the amphibians it parasitizes disappear. Safe reintroduction of a species back to the wild will likely rely on small, cautious releases onto protected land and long-term monitoring. Protecting amphibians against chytrid may be tricky, if not impossible—attempts to immunize the animals would last only a single generation, and fungicides could kill beneficial types and have other unintended consequences. "There will have to be a lot of R&D before reintroduction takes place," Pramuk says.

Before declaring the Ark fully launched, scientists must still clear many hurdles, not the least of which is funding. "Amphibians may not be as charismatic to most people as mammals," Zippel says. "But they are absolutely vital to their ecosystems." Moreover, he adds, because amphibians are sensitive to their environments, "by seeing what happens to them, we might see what's in store for us."

Charles Q. Choi is a freelance writer based in New York City.

FIELD NOTES

Life in Old Lava

Searching for microfossils inside igneous rocks BY CHRISTINA REED

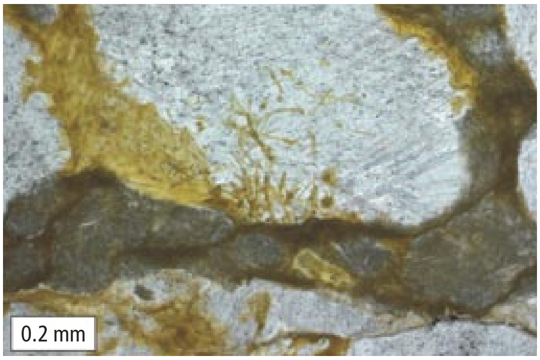
ADORF, GERMANY—After a five-hour drive south from the University of Bremen that got them in at half-past midnight, the two researchers visiting this small village were happy to sit and talk with tavern patrons about the volcano just up the street. Gathered around a map, they listened intently as geobiologists Joern Peckmann and Benjamin Eickmann pointed to the extinct volcano, Arnstein Hill, and explained that the forested region had been underwater 400 million years ago, during the Devonian. Flooded lands were something these German townsfolk could relate to. The completion of the Edersee Dam in 1914 put the neighboring village of Asel at the bottom of a lake.

Peckmann and his students are investigating chemical fossils from the interior of seafloor basalts—solidified lava—from the Devonian. Peckmann, who first reported the findings in March, believes that they have uncovered a previously unknown niche for microbial life, "one that existed in the past, occurs in the present and has the potential to have existed since the beginning of Earth's history," he says. The work could also contribute to investigations of possible fossils in Martian basalt.

Scientists have looked for evidence of life in rocks before but only on the surface of basalt rocks or in sedimentary layers. Igneous rocks, which form under high temperature, are not considered ideal homes. Peckmann is trying to prove otherwise.

On Arnstein Hill, what was once a horizontal seafloor was uplifted to a vertical position and folded multiple times. Rocky outcrops exposed along the face of the cliffs reveal explosions from the Devonian where the lava erupted into the ocean and formed pillow basalts, much like those that form underwater around the shores off Kilauea, Hawaii, today. The seawater quickly cooled the exterior of the lava into a black glass crust of obsidian.

It is this dark rind that Peckmann and Eickmann are looking for as they scramble over boulders and shards along the base of the 60-foot tall cliff. Unlike porous, lightweight pumice, which forms when gas-filled lava cools quickly in the atmosphere, basalt is dense, heavy stuff. Instead of the standard geologic pickax, the researchers carry a sledgehammer. (Only later does Peckmann acknowledge that our hard hats are pretty much useless against any falling basalt bigger than a softball.) After several heavy hits, Eickmann succeeds in breaking open a large sample. Inside, the rock is rife with tiny crystals of carbonate. It is like looking at a loaf of dark German bread baked full of sesame seeds. In the case of the obsidian-crusted pillow basalt, the interior cooled more slowly than the exterior and trapped gas bubbles that later filled with seawater, forming the carbonate crystals, called amygdules, throughout its matrix. "You can't be better protected" than in an amygdule, Peckmann exclaims.



ROCKY EXISTENCE: A slice of 400-million-year-old volcanic rock (*dark band*) has filaments (*yellow*) left behind by microbes that lived inside the rock's pores, now filled in with calcium minerals (*white*).

JOERN PECKMANN *University of Bremen*

Examining thin sections through a microscope reveals tubular or filamentlike growths that branch away from the amygdule walls. These growths are the chemical fossils, molecules that the putative microbes, or cryptoendoliths, produced that are stable over geologic time. Katharina Behrens, one of Peckmann's students, Page Intentionally Blank

is finding similar signs with fresh basalts from Kolbeinsey Ridge in the North Atlantic. In the Devonian rocks chemical analyses revealed that the minerals inside the amygdules precipitated from seawater, rather than from hydrothermal fluid, which is hostile to life. This is key for convincing others that the microbes were using the basalt as a home.

Although other scientists have found microbes boring into the glassy rinds before, the work by Peckmann and his colleagues marks "the first time that apparently mineralized microbial filaments have been found in gas vesicles" and voids in basalts, says astrobiologist Roger Buick of the University of Washington. "Thus, the study suggests a new style of preservation for microbial fossils" that could potentially be applied to older rocks, thereby "providing scientists with new tools to search for signs of life very early in Earth's history." Moreover, because basalts are common on Mars, the techniques "could even be applied to the search for extraterrestrial fossilized life," Buick remarks.

At the Arnstein outcrop, something else now claimed the pillow basalts for a home. During the examination of an outcrop, human voices startled a large owl that flew silently away. Peckmann identified the owl as an uhu, an endangered species. "Time for us to leave," he said. Two small chicks looking more like a leftover bundle of fluff awaited their mother's return. The pillow basalts, it seems, are still providing ecological niches.

Christina Reed is working on a book about the origin of life.

Q&A WITH ISABELLA ROSSELLINI

A Bug's Sex Life

A humanized view of invertebrate love BY CHARLES Q. CHOI

Isabella Rossellini, well known as a supermodel and movie star, is now making short films for mobile devices that illustrate the sex lives of dragonflies, earthworms and other creatures. But they are not like standard nature shows. In these films, which she researched with the help of Wildlife Conservation Society experts, she not only details unusual aspects of the critters' biology but also dresses up as them and mimics sex with paper cutouts. We asked Rossellini what she hopes to accomplish with the films on invertebrate love, dubbed *Green Porno,* which premiered May 5 on the Sundance Channel's Web site.

How did you get started making these short films?

Sundance was interested in experimenting and expanding the definition of film. Sundance said, "Would you be interested in making films for the mobile?" We thought short films would be something that people would dedicate two minutes to watch, but longer would be difficult.

You call it *Green Porno*—what's the story behind the name?

Sundance wanted, if possible, content that was environmental, because the channel and Robert Redford [the creative director of the network] are very dedicated to it. And then they said, "Because this is new media, can you make it flashy and funny?" Flashy to me translated into sex, so it's great to do a very short little series about the life of bugs.

Was it hard researching the sexual behavior of bugs?

It was difficult. I was always joking with some of the scientists I called that when it comes to insects, you can go through pages and pages and pages of how their mouths work, and I kept on saying, "I want to know how the genitalia work."

SUNDANCE CHANNEL

BUG PORN: Isabella Rossellini acts out apiary mating behaviors for mobile screens.

There are great descriptions about mouths and not much about sex.

I read scientific books that have a lot of terminology that is hard for me to understand. So I bring it back to humans. That's the process I tried to illustrate when I did *Green Porno*. I was terrified of making mistakes. I'm a very big supporter of the Wildlife Conservation Society, so I kept calling them, and their scientists are very kind.

How far did you go with the costumes?

Often I had the bug eyes. Once I have the eyes on, I can't see anything. But the earthworm was the worst, because the costume is 35 feet long. Once I was in the costume I couldn't come out, and then my arms were along my body, so I was completely strapped, and it's very constrictive. I almost broke out of it one afternoon after being there for three hours while they were fiddling with the lights for some reason—"Ahh, I can't wait, I'm going nuts!" They [the costumes] were fragile. Once I humped them, they came apart [*laughs*].

You also play the males quite often—for instance, in one of the shorts, you portray a small male spider that sneaks up to mate with a large female to avoid getting eaten.

Obviously, there are lots of species of spiders, and I had to generalize there—spiders have the most incredible sexual rituals. If I do another series [of films], I might have to add more spiders—they do things that are very funny.

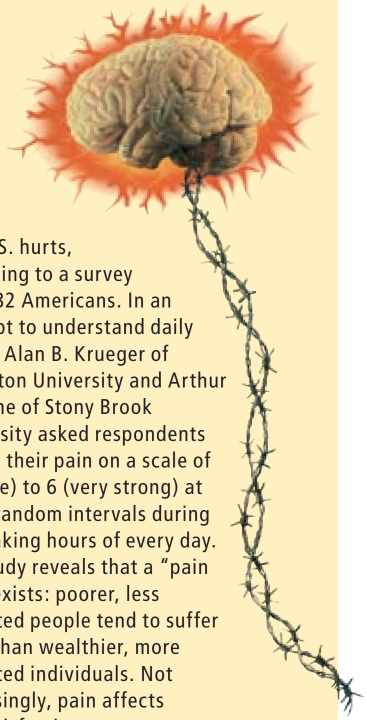
So why focus on insects as opposed to the rest of the animal kingdom?

Mammals would look too pornographic. With the bugs, they're so strange and far out, they're comical. If a human being behaved like a bug, he or she would be arrested.

Also, when I was little, I always said I should have been born in Africa or been like Jane Goodall. That was my dream. And then when I moved to live in the country, I discovered all these bugs in my backyard. I discovered you can do your own safari. Animals are everywhere. Some are more romantic, like tigers and elephants and chimpanzees, and some are less romantic, like earthworms, but they are just as interesting.

Charles Q. Choi is a frequent contributor. An expanded version of his interview with Rossellini is at **www.SciAm.com/jul2008**

Data Points
People in Pain



The U.S. hurts, according to a survey of 3,982 Americans. In an attempt to understand daily aches, Alan B. Krueger of Princeton University and Arthur A. Stone of Stony Brook University asked respondents to rate their pain on a scale of 0 (none) to 6 (very strong) at three random intervals during the waking hours of every day. The study reveals that a "pain gap" exists: poorer, less educated people tend to suffer more than wealthier, more educated individuals. Not surprisingly, pain affects life satisfaction.

Percent of Americans in pain at any given time: 28

PERCENT OF THOSE IN PAIN WHO:

Earn less than $30,000: 34.2
Earn more than $100,000: 22.9

Did not finish high school: 33
Got a college degree: 20.2

Are not satisfied with life: 53.9
Average pain rating: 2.26

Are very satisfied with life: 22.4
Average pain rating: 0.66

AMOUNT SPENT ANNUALLY ON:

Nonprescription painkillers: $2.6 billion
Outpatient prescription painkillers: $13.8 billion
Productivity lost annually because of pain: $60 billion

SOURCE: Lancet, *May 3, 2008*

ECOLOGY
Eating with Tension

PHALAROPE, a shorebird, relies on the surface tension of water to feed.

The long, thin beaks of shorebirds called phalaropes are no good at sucking up water and any tasty crustaceans within. Instead they rely on the attractive force of liquid known as surface tension to ferry prey upward. The birds first swim in small, fast circles on the surface of the water, creating a vortex that pulls creatures up within their reach. They next peck at the water and then rapidly open and close their beaks. This scissoring motion both pulls and squeezes droplets, about two millimeters in size, and moves them from the tip of their beaks into their mouths. In experiments with mechanical beaks, scientists at the Massachusetts Institute of Technology and the French National Center for Scientific Research find that the droplets do not move well if the water contains oil, detergents and other pollutants that alter water's surface tension. Draw in the findings from the May 16 *Science*. *—Charles Q. Choi*

ONCOLOGY
Cancerous Marriage

The fusion of tumor cells with white blood cells may be the secret behind how cancer spreads around the body. Such hybrids can combine white blood cells' natural ability to migrate with cancer's proclivity for uncontrolled cell division. The fusion theory was first proposed in the early 1900s. In research spanning 15 years, Yale University scientists merged white blood cells with tumor cells, leading to remarkably metastatic hybrids that were lethal when implanted into mice. They later found that such hybrids occur naturally in mice. In recent studies of cancer patients who received a bone marrow transplant, genes from the marrow's white blood cells were found in the patient's tumor cells. Such fusion might occur after white blood cells engulf tumor cells. By viewing this fusion as another disease imposed onto tumor cells, scientists could devise new therapies against metastasis, the researchers say in the May *Nature Reviews Cancer*. *—Charles Q. Choi*

IMMUNOLOGY
A Milk-Diabetes Connection?

Some research has suggested formula containing cow's milk protein could raise an infant's risk of later acquiring type 1 diabetes. A new study by Marcia F. Goldfarb of Anatek-EP, a protein research laboratory in Portland, Me., posits a mechanism that may be at play. She notes that a newborn's immature immune system may destroy the human protein glycodelin in a mistaken effort to eliminate the similar cow's milk protein. This error could result in the overproduction of T cells, which help to protect the body against infections. The overproduction could attack the insulin-producing cells of the pancreas and trigger diabetes, she wrote in the June 6 *Journal of Proteome Research* of the American Chemical Society. A large, international randomized trial called TIGR now under way should help settle the question of cow's milk and diabetes risk.

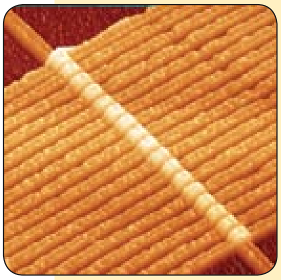
—Keren Blankfeld Schultz

WILDLIFE/PETER ARNOLD, INC. (*bird*); ALTRENDO IMAGES/GETTY IMAGES (*baby*); ILLUSTRATION BY MATT COLLINS

In Brief

MEMRISTOR MADE

After nearly 40 years, scientists have constructed a new addition to the stable of circuit elements (inductors, capacitors and resistors). Called the memristor, or memory resistor, it is a nanometer-scale electric switch that "remembers" whether it is on or off after its power is turned off. It might become a useful tool for constructing nonvolatile computer memory or for packing transistors together more densely to make smaller chips. A Hewlett-Packard team crafted the device by inserting a layer of titanium dioxide as thin as three nanometers between a pair of platinum layers. *—JR Minkel*



MEMRISTORS, 17 in all, were made with 50-nanometer-wide platinum wires crossed by another wire.

CONCRETE MATH LEARNING

Abstract examples are more effective than practical problems for teaching math concepts. Researchers at the Ohio State University taught one group of students a new mathematical system using symbols, such as circles and diamonds, and another group using scenarios, such as combining liquids in measuring cups. Students who learned using symbols scored 80 percent on a test requiring them to apply their knowledge in a novel situation; the others scored between 40 and 50 percent. *—Nikhil Swaminathan*

TOASTED BUGS

Although climate change will likely raise temperatures more in temperate and polar regions than in equatorial zones, tropical insects may suffer more than their counterparts in cooler climes. Used to thriving in a narrow temperature range, tropical insects may be more sensitive to shifts—they already live in conditions that verge on being too hot for them, a recent study finds. Insects in temperate areas, however, will probably thrive with an extra bit of warming. *—David Biello*

PRIVACY

GINA Becomes Genuine

By late May, President George W. Bush was expected to have signed into law the Genetic Information Nondiscrimination Act (GINA), which will prohibit health insurers from canceling or denying coverage or hiking premiums based on a genetic predisposition to a specific disease. The legislation, which sailed through the House and Senate, also bars employers from using genetic data to hire, fire, promote or make other employment-related decisions.

The measure caps more than a decade of political wrangling: Representative Louise Slaughter of New York introduced the first genetic antidiscrimination legislation 13 years ago. In the past, genetic discrimination has played a role in preventing many Americans from obtaining work or seeking health treatments. In the 1970s, for instance, many African-Americans were denied jobs and insurance coverage because they carried a gene for sickle-cell anemia. Physicians now have access to at least 1,000 genetic tests that diagnose or assess the risk of developing potentially life-threatening diseases, including breast cancer, diabetes, heart disease and Parkinson's.

—JR Minkel and Lisa Stein

NEUROSCIENCE

Preemptive Strike against Mindless Mistakes

Everyone has had the mindless slipup during a monotonous task. A lapse in concentration or brain activity, however, is not the sole culprit for that slip. In fact, activity patterns occurring in a set of brain regions associated with maintaining task effort can be used to forecast flawed behavior up to 30 seconds before it occurs, possibly preventing the imminent errors. Researchers at the University of Bergen in Norway used functional MRI to scan the brains of individuals performing a simple tedious task—in this case, determining the correct directions of arrows on a computer screen.

Activity in the brain's task-performing network decreased before a mistake occurred, and once the individuals detected their mistake, they reengaged, resetting the activity pattern. According to lead researcher Tom Eichele, the next step in predicting mindless errors will be through the use of electroencephalography, a technology that is portable and wireless and can make the predictions more practically applicable. The study appears in the April 22 *Proceedings of the National Academy of Sciences USA*. *—Keren Blankfeld Schultz*

A DULL JOB can produce mindless errors.

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COURTESY OF J. J. YANG *HP Labs* (memristors); ALEX MALONEY *zefa/Corbis* (worker)

SciAm Perspectives

Private, Historical and Genetic Truths

New legislation shields some genetic secrets—time and mistrust still obscure others

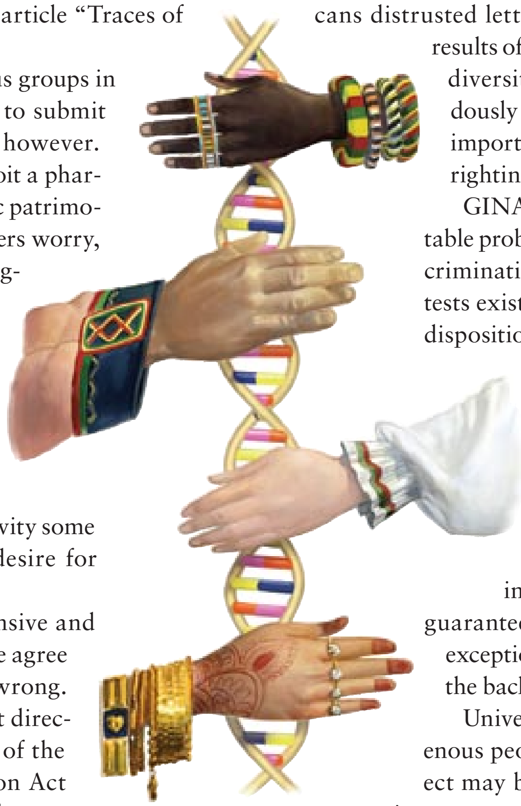
BY THE EDITORS

When our ancient ancestors migrated out of Africa and throughout the rest of the world, telltale variations in the DNA of the people who settled along the way marked their passage. Today anthropologists and molecular biologists of the Genographic Project, sponsored by the National Geographic Society and others, seek to reconstruct the forgotten migration routes by looking for those genetic "footprints," as senior writer Gary Stix relates in his article "Traces of a Distant Past," beginning on page 56.

The unwillingness of many indigenous groups in Australia, the Americas and elsewhere to submit DNA samples has hindered progress, however. Some worry that industrialists will exploit a pharmaceutically useful detail of their genetic patrimony and pay them nothing for it. Still others worry, with good cause, that information emerging from the studies might contradict their cultural traditions about their origins (Native Americans who believe their people have always occupied certain lands do not welcome the suggestion that their ancestors came from Siberia 13,000 years ago). Given the long histories of oppression and insensitivity some of those groups have suffered, their desire for genetic privacy is understandable.

The issue of genetic privacy is expansive and complicated, but most reasonable people agree that discrimination based on genes is wrong. Happily, the U.S. took a step in the right direction in April with the overdue passage of the Genetic Information Nondiscrimination Act (GINA) after 13 years of congressional wrangling. GINA, which closes holes in the interpretation of the Americans with Disabilities Act, prohibits the misuse of gene tests by health insurers to deny coverage or by employers when hiring, firing or making promotion decisions.

Opponents of GINA, who were primarily from industry, had argued that the act was too broad and redundant with legal protections at the state level and would be prohibitively expensive. They pointed out that it is rare to encounter the genetic discrimination that GINA is designed to prevent: insurers still rely mostly on personal and family medical histories rather than on genetic tests in making coverage decisions.



MATT COLLINS

Nevertheless, GINA may be worthwhile if only for the sake of allaying public fears. A 2007 survey by the Genetics and Public Policy Center found that nearly three out of four Americans distrusted letting insurers and employers know the results of their gene tests. Both the frequency and diversity of tests will likely expand tremendously in years to come. GINA might be more important for preventing future abuse than for righting current wrongs.

GINA has its limits, however. The least tractable problem is that the incentives for genetic discrimination can run deep. After all, many gene tests exist precisely because they do identify predispositions for potential medical problems. As long as it is rational for insurers to use genetic information to exclude certain people from coverage or for employers to use it in hiring decisions, they will keep trying to find ways to do so. In the U.S., the best strategy for attacking genetic discrimination at its root may be to provide fuller guarantees of health care for everyone without exception. That would get health insurance off the backs of individuals and employers alike.

Universally allaying the misgivings of indigenous peoples who resist the Genographic Project may be impossible, but that does not mean stepwise progress is. Geneticist Sarah A. Tishkoff of the University of Pennsylvania obtained samples from 100 ethnic groups by spending a decade in the field gaining the trust of village leaders throughout East and West Africa. Fundamentally, the problems of the gene researchers echo the distrust born of the groups' experience. Thousands of years of history separated these peoples in the first place—researchers will not be able to brush past the consequences of that legacy overnight. ■

Sustainable Developments

A Deadline on Malaria

The challenge of controlling the disease in Africa by 2010 is fundamentally organizational, not technical

BY JEFFREY D. SACHS

In a dramatic call to action in April, United Nations secretary-general Ban Ki-moon—backed by the African Union, the World Health Organization, UNICEF, the Gates Foundation, ExxonMobil, the World Bank, and the Global Fund to Fight AIDS, Tuberculosis and Malaria, among other key international organizations and businesses—set a timetable for comprehensive malaria control in Africa by the end of 2010. Secretary-General Ban has thrown down the gauntlet: there is no reason why a million or more children should die every year of a largely preventable and wholly treatable disease.

The operational objective is to ensure that crucial interventions are taken continent-wide and at the appropriate scale within the next two and a half years. As I described in this space in October 2007, the package of technical control measures is now settled. There should be restriction of the mosquito vector (especially through the use of insecticide-treated bed nets and indoor spraying of insecticides); timely treatment of every clinical case with effective medicines; preventive treatment for pregnant women; and trained community health workers who will link clinics and communities in rural areas. In view of the lives to be saved and the economic benefits of reining in the disease, the total cost of around $3 billion a year is one of the world's great bargains.

The main challenge will therefore be organizational rather than conceptual or scientific. Many skeptics doubt that this kind of program can work, much less on an accelerated timetable. The international system is a congeries of overlapping public and private institutions without clear mandates, ease of coordination or a single "conductor" to harmonize activities. Many of these institutions are sporadically funded. The recipient governments are not always noted for their transparency, efficiency and accountability, to say the least.

Yet the chances for success are also strong. Many African leaders have long been committed to this fight. The U.N. secretary-general and the office of his special envoy on malaria represent a clear point of leadership. The Global Fund to Fight AIDS, Tuberculosis and Malaria serves as a dominant funding organization. Happily, the U.S. government is committed to its own sizable contribution, which will likely grow in view of robust congressional support. Finally, the Roll Back Malaria Partnership has had years of experience in bringing the multitude of "partner institutions" under one roof.

The needed technologies are relatively straightforward and much easier to use than those, for example, for controlling the HIV/AIDS pandemic. Bed nets and antimalaria medicines could be deployed rapidly to good effect. We may also take heart in the success of an immunization campaign in reducing the number of deaths from measles in Africa by more than 90 percent since the year 2000. Other recent triumphs include the control of polio, leprosy and guinea worm.

Still, the timing will be very tight and will require an unprecedented degree of coordination among financing, training, monitoring and logistics. Each sub-Saharan country will need to adopt, vet, fund and monitor a scaled-up antimalaria plan very quickly. The major global manufacturers of commodities such as bed nets, antimalaria drugs and diagnostics will have to raise production to hundreds of millions of units. Tens or hundreds of thousands of community health workers will need weeks of training.

The stakes are exceedingly high. Not just millions of lives but also the very capacity of the world to take on big and crucial goals is at stake. In the case of malaria, we can restore health and unleash massive economic gain, but only if countless agencies, dozens of countries and hundreds of millions of individuals can effectively take a shared action. Success will enable us to consider similarly urgent challenges in food production, water management, biodiversity conservation and climate control, to name but four crucial areas. The consequences of failure, on the other hand, would be almost too painful to behold. The countdown to 2010 has begun. ■

Jeffrey D. Sachs is director of the Earth Institute at Columbia University (www.earth.columbia.edu).

An extended version of this essay is available at **www.SciAm.com/jul2008**

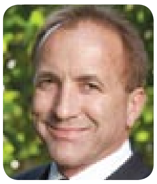
PHOTOGRAPH BY BRUCE GILBERT/EARTH INSTITUTE; ILLUSTRATION BY MATT COLLINS

Skeptic

Sacred Science

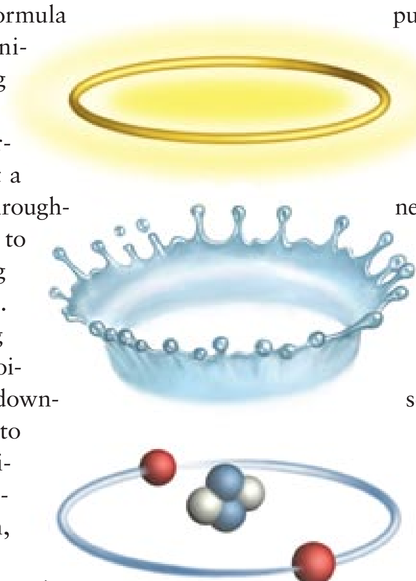
Can emergence break the spell of reductionism and put spirituality back into nature?

BY MICHAEL SHERMER



In the early 17th century a demon was loosed on the world by Italian mathematician Galileo Galilei when he began swinging pendulums, rolling balls down ramps and observing the moons of Jupiter—all with an aim toward discovering regularities that could be codified into laws of nature.

So successful was this mechanical worldview that by the early 19th century French mathematician Pierre-Simon Laplace was able to "imagine an Intelligence who would know at a given instant of time all forces acting in nature and the position of all things of which the world consists.... Then it could derive a result that would embrace in one and the same formula the motion of the largest bodies in the universe and of the lightest atoms. Nothing would be uncertain for this Intelligence."



By the early 20th century science undertook to become Laplace's demon. It cast a wide "causal net" linking effects to causes throughout the past and into the future and sought to explain all complex phenomena by reducing them into their simpler component parts. Nobel laureate physicist Steven Weinberg captured this philosophy of reductionism poignantly: "All the explanatory arrows point downward, from societies to people, to organs, to cells, to biochemistry, to chemistry, and ultimately to physics." In such an all-encompassing and fully explicable cosmos, then, what place for God?

Stuart Kauffman has an answer: naturalize the deity. In his new book, *Reinventing the Sacred* (Basic Books, 2008), Kauffman—founding director of the Institute for Biocomplexity and Informatics at the University of Calgary in Alberta and one of the pioneers of complexity theory—reverses the reductionist's causal arrow with a comprehensive theory of emergence and self-organization that he says "breaks no laws of physics" and yet cannot be explained by them. God "is our chosen name for the ceaseless creativity in the natural universe, biosphere and human cultures," Kauffman declares.

In Kauffman's emergent universe, reductionism is not wrong so much as incomplete. It has done much of the heavy lifting in the history of science, but reductionism cannot explain a host of as yet unsolved mysteries, such as the origin of life, the biosphere, consciousness, evolution, ethics and economics. How would a reductionist explain the biosphere, for example? "One approach would be, following Newton, to write down the equations for the evolution of the biosphere and solve them. This cannot be done," Kauffman avers. "We cannot say ahead of time what novel functionalities will arise in the biosphere. Thus we do not know what variables—lungs, wings, etc.—to put into our equations. The Newtonian scientific framework where we can prestate the variables, the laws among the variables, and the initial and boundary conditions, and then compute the forward behavior of the system, cannot help us predict future states of the biosphere."

This problem is not merely an epistemological matter of computing power, Kauffman cautions; it is an ontological problem of different causes at different levels. Something wholly new emerges at these higher levels of complexity.

Similar ontological differences exist in the self-organized emergence of consciousness, morality and the economy. In my recent book, *The Mind of the Market* (Times Books, 2008), I show how economics and evolution are complex adaptive systems that learn and grow as they evolve from simple to complex and how they are autocatalytic, or containing self-driving feedback loops. It was therefore gratifying to find corroboration in Kauffman's detailed explication of why such phenomena "cannot be deduced from physics, have causal powers of their own, and therefore are emergent real entities in the universe." This creative process of emergence, Kauffman contends, "is so stunning, so overwhelming, so worthy of awe, gratitude and respect, that it is God enough for many of us. God, a fully natural God, is the very creativity in the universe."

I have spent time with Stu Kauffman at two of the most sacred places on earth: Cortona, Italy (under the Tuscan sun), and Esalen, Calif. (above the Pacific Ocean), at conferences on the intersection of science and religion. He is one of the most spiritual scientists I know, a man of inestimable warmth and ecumenical tolerance, and his God 2.0 is a deity worthy of worship. But I am skeptical that it will displace God 1.0, Yahweh, whose Bronze Age program has been running for 6,000 years on the software of our brains and culture. ■

Michael Shermer is publisher of Skeptic *(www.skeptic.com).*

PHOTOGRAPH BY BRAD SWONETZ; ILLUSTRATION BY MATT COLLINS

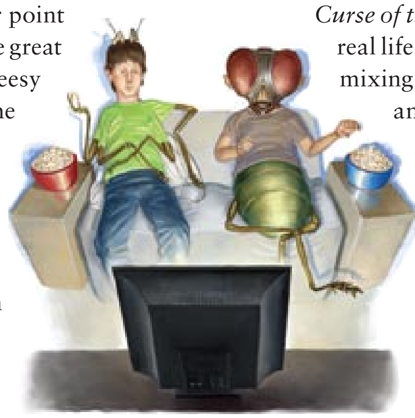
Anti Gravity

The Joys of Summarized Cinema

Quick flick descriptions for the inveterate channel surfer

BY STEVE MIRSKY

Remember *The Fly* movies? A visionary researcher attempts to build a *Star Trek*–like transporter. But human bits mix with bits of the fly that happen to be in the machine. Result: flyman or manfly depending on your point of view. I actually prefer the great Vincent Price effort of 1958, in which a cheesy fly head is perched on a human body. And the fly's body carries a tiny human head that squeaks, "Help me!" The 1986 Jeff Goldblum version of *The Fly* is creepier, because, well, it stars Jeff Goldblum. Also, the integration of fly and human is more complex, because their DNA appears to have gotten mixed. Of course, there are 10 times as many microbial cells as human cells in and on any of us, and none of that DNA seems to get mixed up with Goldblum. Possibly because nobody was going to go see a movie called *The E. Coli*.



Anyway, I was channel surfing recently and happened on a listing for one of the lesser works in the fly chronicles, the 1965 *Curse of the Fly*. (Which starred Brian Donlevy. Who in real life was the stepfather of Bela Lugosi, Jr. Which is mixing apples and oranges. If by apples you mean flies and by oranges you mean bats.) And I became intrigued by the short description of *Curse of the Fly* that appeared on the screen when I hit the info button on the remote: "A mad scientist tries out a molecular disintegrator on people but cannot get the hang of it."

It occurred to me that other sci-fi and fantasy movies also require terse synopses for the channel-surfing community. Here then is a selection of such possible descriptions:

2001: A Space Odyssey
A slab of onyx and a singing computer get two astronauts in hot water.

Alien
A feisty cat survives tense times onboard a spaceship.

The Day the Earth Stood Still
A drifter helps an old man with his math problems.

Close Encounters of the Third Kind
Frail aliens visit Earth in search of clothing, music, friends and possibly gym equipment.

Starship Troopers
Valiant insects try to repel totalitarian invaders.

E.T. the Extra-Terrestrial
A nerd from another planet goes bike riding and trick-or-treating.

Stargate
Kurt Russell and his buzz cut outwit the guy who played the girl who was a guy in *The Crying Game*.

Predator
The future governor of California and the future governor of Minnesota go hiking.

Indiana Jones and the Kingdom of the Crystal Skull
An archaeology professor searches for his college's retirement buyout and a good rheumatologist.

Star Trek IV: The Voyage Home
Kirk, Spock and McCoy blend right in while visiting late 20th-century San Francisco.

Robot Monster
A guy in a gorilla suit and diving helmet with rabbit-ear antennas walks up and down a hillside for no apparent reason.

Iron Man
An arms manufacturer finds himself neck-deep but gets a leg up and heads home.

The Matrix
A man discovers his true destiny.

Star Wars
An adolescent discovers his true destiny.

Harry Potter and the Sorcerer's Stone
A boy discovers his true destiny.

Lord of the Rings: The Fellowship of the Ring
A hobbit discovers his true destiny.

Expelled: No Intelligence Allowed
A sad sack seeks a way to turn back time so he can live in the Dark Ages.

PHOTOGRAPH BY FLYNN LARSEN; ILLUSTRATION BY MATT COLLINS

PHYSICS

The Self-Organizing QUANTUM

KEY CONCEPTS

- Quantum theory and Einstein's general theory of relativity are famously at loggerheads. Physicists have long tried to reconcile them in a theory of quantum gravity—with only limited success.
- A new approach introduces no exotic components but rather provides a novel way to apply existing laws to individual motes of spacetime. The motes fall into place of their own accord, like molecules in a crystal.
- This approach shows how four-dimensional spacetime as we know it can emerge dynamically from more basic ingredients. It also suggests that spacetime shades from a smooth arena to a funky fractal on small scales.

—The Editors

A new approach to the decades-old problem of quantum gravity goes back to basics and shows how the building blocks of space and time pull themselves together

By Jan Ambjørn, Jerzy Jurkiewicz and Renate Loll

How did space and time come about? How did they form the smooth four-dimensional emptiness that serves as a backdrop for our physical world? What do they look like at the very tiniest distances? Questions such as these lie at the outer boundary of modern science and are driving the search for a theory of quantum gravity—the long-sought unification of Einstein's general theory of relativity with quantum theory. Relativity theory describes how spacetime on large scales can take on countless different shapes, producing what we perceive as the force of gravity. In contrast, quantum theory describes the laws of physics at atomic and subatomic scales, ignoring gravitational effects altogether. A theory of quantum gravity aims to describe the nature of spacetime on the very smallest scales—the voids in between the smallest known elementary particles—by quantum laws and possibly explain it in terms of some fundamental constituents.

Superstring theory is often described as the leading candidate to fill this role, but it has not yet provided an answer to any of these pressing questions. Instead, following its own inner logic, it has uncovered ever more complex layers of new, exotic ingredients and relations among them, leading to a bewildering variety of possible outcomes.

Over the past few years our collaboration has developed a promising alternative to this much traveled superhighway of theoretical physics. It follows a recipe that is almost embarrassingly simple: take a few very basic ingredients, assem-

JEAN-FRANCOIS PODEVIN

ble them according to well-known quantum principles (nothing exotic), stir well, let settle—and you have created quantum spacetime. The process is straightforward enough to simulate on a laptop.

To put it differently, if we think of empty spacetime as some immaterial substance, consisting of a very large number of minute, structureless pieces, and if we then let these microscopic building blocks interact with one another according to simple rules dictated by gravity and quantum theory, they will spontaneously arrange themselves into a whole that in many ways looks like the observed universe. It is similar to the way that molecules assemble themselves into crystalline or amorphous solids.

Spacetime, then, might be more like a simple stir fry than an elaborate wedding cake. Moreover, unlike other approaches to quantum gravity our recipe is very robust. When we vary the details in our simulations, the result hardly changes. This robustness gives reason to believe we are on the right track. If the outcome were sensitive to where we put down each piece of this enormous ensemble, we could generate an enormous number of baroque shapes, each a priori equally likely to occur—so we would lose all explanatory power for why the universe turned out as it did.

Similar mechanisms of self-assembly and self-organization occur across physics, biology and other fields of science. A beautiful example is the behavior of large flocks of birds, such as European starlings. Individual birds interact only with a small number of nearby birds; no leader tells them what to do. Yet the flock still forms and moves as a whole. The flock possesses collective, or emergent, properties that are not obvious in each bird's behavior.

A Brief History of Quantum Gravity

Past attempts to explain the quantum structure of spacetime as a process of emergence had only limited success. They were rooted in Euclidean quantum gravity, a research program initiated at the end of the 1970s and popularized by physicist Stephen Hawking's best-selling book *A Brief History of Time*. It is based on a fundamental principle from quantum mechanics: superposition. Any object, whether a classical or quantum one, is in a certain state—characterizing its position and velocity, say. But whereas the state of a classical object can be described by a unique set of numbers, the state of a quantum object is far richer. It is the sum, or superposition, of all possible classical states.

For instance, a classical billiard ball moves along a single trajectory with a precise position and velocity at all times. That would not be a good description for how the much smaller electron moves. Its motion is described by quantum laws, which imply that it can exist simultaneously in a wide range of positions and velocities. When an electron travels from point A to point B in the absence of any external forces, it does not just take the straight line between A and B but all available routes simultaneously. This qualitative picture of all possible electron paths conspiring together translates into the precise mathematical prescription of a quantum superposition, formulated by Nobel laureate Richard Feynman, which is a weighted average of all these distinct possibilities.

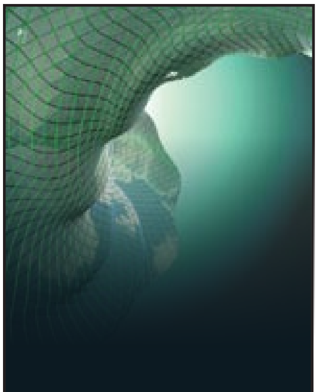
With this prescription, one can compute the probability of finding the electron in any particular range of positions and velocities away from the straight path that we would expect if the electrons followed the laws of classical mechanics. What makes the particles' behavior distinctly quantum mechanical are the deviations from a single sharp trajectory, called quantum fluctuations. The smaller the size of a physical system one considers, the more important the quantum fluctuations become.

Euclidean quantum gravity applies the superposition principle to the entire universe. In this case, the superposition consists not of different particle paths but of different ways the entire universe could evolve in time—in particular, the various possible shapes of spacetime. To make the problem tractable, physicists typically consider only the general shape and size of spacetime, rather than every single one of its conceivable contortions [see "Quantum Cosmology and the Creation of the Universe," by Jonathan J. Halliwell; Scientific American, December 1991].

Euclidean quantum gravity took a big technical leap during the 1980s and 1990s with the development of powerful computer simulations. These models represent curved spacetime geometries using tiny building blocks, which, for convenience, are taken to be triangular. Triangle meshes can efficiently approximate curved surfaces, which is why they are frequently used in computer animations. For spacetime, the elementary building blocks are four-dimensional generalizations of triangles, called four-simplices. Just as gluing together triangles at their edges creates a two-dimensional curved surface, gluing four-simplices along their "faces" (which are actually three-dimensional tetrahedra) can produce a four-dimensional spacetime.

The tiny building blocks themselves have no direct physical meaning. If one could examine real spacetime with an ultrapowerful microscope, one would not see small triangles. They are merely approximations. The only physically relevant information comes from the collective behavior of the building blocks imagining that each one is shrunk down to zero size. In this limit, nothing depends on whether the blocks were triangular, cubic, pentagonal or any mixture thereof to start with.

The insensitivity to a variety of small-scale details also goes under the name of "universality." It is a well-known phenomenon in statistical mechanics, the study of molecular motion in gases and fluids; these substances behave much the same whatever their detailed composition is. Universality is associated with properties of systems of many interacting parts and shows up on a scale much larger than that of the individual constituents. The analogous statement for a flock of starlings is that the color, size, wingspan and age of individual birds are completely



THEORIES OF QUANTUM GRAVITY

STRING THEORY
The approach favored by most theoretical physicists, it is a theory not just of quantum gravity but of all matter and forces. It is based on the idea that particles (including the hypothetical ones that transmit gravity) are vibrating strings.

LOOP QUANTUM GRAVITY
The main alternative to string theory, it invokes a new technique for applying quantum rules to Einstein's general theory of relativity. Space is divided into discrete "atoms" of volume.

EUCLIDEAN QUANTUM GRAVITY
Made famous by physicist Stephen Hawking, this approach supposes that spacetime emerges from a grand quantum average of all possible shapes. It puts time on the same footing as space.

CAUSAL DYNAMICAL TRIANGULATIONS
This approach, the subject of this article, is a modern version of the Euclidean approach. It approximates spacetime as a mosaic of triangles, which have a built-in distinction between space and time. On small scales, spacetime takes on a fractal shape.

[SLALOMING THROUGH SPACE]

Space: The Final Frontier

Although we usually think of space as mere void, both it and time have an invisible structure that guides how we move—much as the moguls (bumps) on a slope guide a skier. We perceive this structure as the force of gravity. Explaining the detailed shape of spacetime is the main goal of a theory of quantum gravity.

JEAN-FRANCOIS PODEVIN; KARL WEATHERLY *Corbis (mogul skier)* irrelevant in determining the flying behavior of the flock as a whole. Only a few microscopic details filter through to macroscopic scales.

Shriveling Up

With these computer simulations, quantum gravity theorists began to explore the effects of superposing spacetime shapes that classical relativity cannot handle—specifically, ones that are highly curved on very small distance scales. This so-called nonperturbative regime is precisely what physicists are most interested in but is largely inaccessible with the usual pen-and-paper calculations.

Unfortunately, these simulations revealed that Euclidean quantum gravity is clearly missing an important ingredient somewhere along the line. They found that nonperturbative superpositions of four-dimensional universes are inherently unstable. The quantum fluctuations of curvature on short scales, which characterize the different superposed universes contributing to the average, do not cancel one another out to produce a smooth, classical universe on large scales. Instead they typically reinforce one another to make the entire space crumple up into a tiny ball with an infinite number of dimensions. In such a space, arbitrary pairs of points are never more than a tiny distance apart, even if the space has an enormous volume. In some instances, space goes to the other extreme and becomes maximally thin and extended, like a chemical polymer with many branches. Neither of these possibilities remotely resembles our own universe.

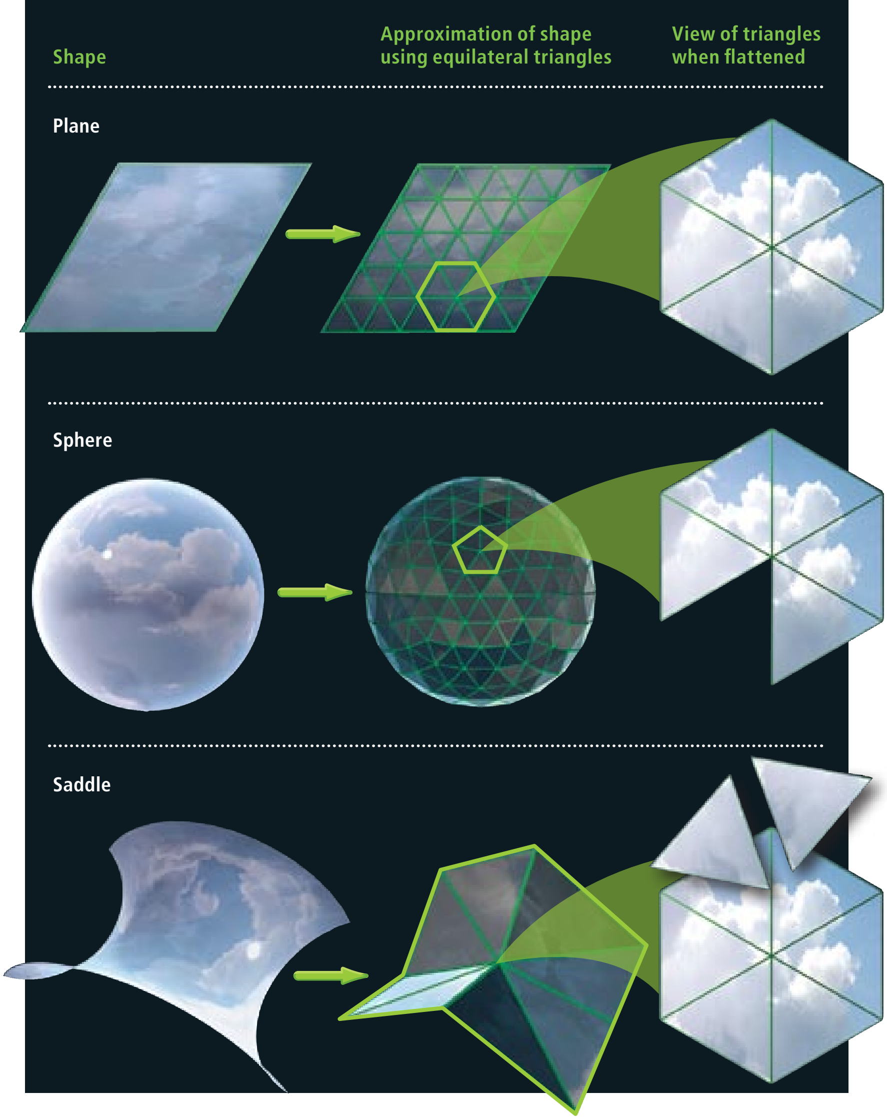
Before we reexamine the assumptions that led physicists down this dead-end street, let us pause to consider an odd aspect of this result. The building blocks are four-dimensional, yet they collectively give rise to a space having an infinite number of dimensions (the crumpled universe) or two dimensions (the polymer universe). Once the genie is let out of the bottle by allowing large quantum fluctuations of empty space, even a very basic notion such as dimension becomes changeable. This outcome could not possibly have been anticipated from the classical theory of gravity, in which the number of dimensions is always taken as a given.

One implication may come as a bit of a disappointment to science-fiction aficionados. Science-fiction stories commonly make use of wormholes—thin handles attached to the universe that provide a shortcut between regions that would otherwise be far apart. What makes wormholes so exciting is their promise of time travel and faster-than-light transmission of signals. Although such phenomena have never been observed, physicists have speculated that wormholes might find a justification within the still unknown theory of quantum gravity. In view of the negative results from the computer simulations of Euclidean quantum gravity, the viability of wormholes now seems exceedingly unlikely. Wormholes come in such a huge variety that they tend to dominate the superposition and destabilize it, and so the quantum universe never gets to grow beyond a

[DESCRIBING THE SHAPE OF SPACE]

A Mosaic of Triangles

To determine how space sculpts itself, physicists first need a way to describe its shape. They do so using triangles and their higher-dimensional analogues, a mosaic of which can readily approximate a curved shape. The curvature at a point is reflected in the total angle subtended by the triangles that surround it. For a flat surface, the angle is exactly 360 degrees, but for curved surfaces it can be less or more.

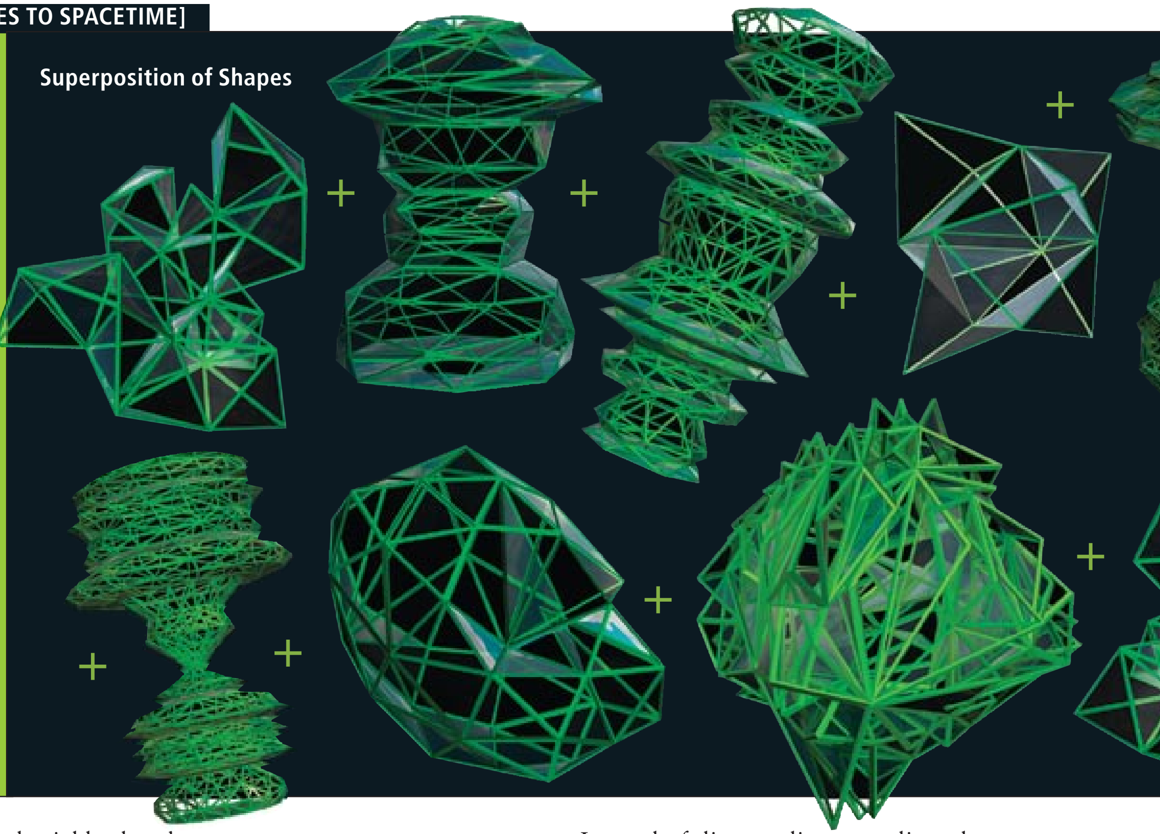


JEAN-FRANCOIS PODEVIN

[APPLYING QUANTUM RULES TO SPACETIME]

Taking the Average

Spacetime can take on a huge number of possible shapes. According to quantum theory, the shape we are most likely to observe is a superposition, or weighted average, of all these possibilities. When constructing shapes from triangles, theorists weight each shape depending on how exactly they glue together triangles to form it. The authors have discovered that the triangles must follow certain rules for the average to match what we observe. In particular, the triangles must have a built-in arrow of time.



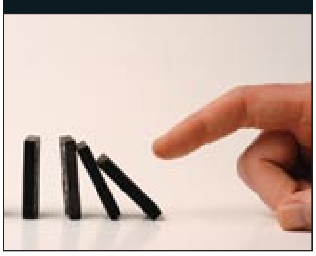
small but highly interconnected neighborhood.

What could the trouble be? In our search for loopholes and loose ends in the Euclidean approach, we finally hit on the crucial idea, the one ingredient absolutely necessary to make the stir fry come out right: the universe must encode what physicists call causality. Causality means that empty spacetime has a structure that allows us to distinguish unambiguously between cause and effect. It is an integral part of the classical theories of special and general relativity.

Euclidean quantum gravity does not build in a notion of causality. The term "Euclidean" indicates that space and time are treated equally. The universes that enter the Euclidean superposition have four spatial directions instead of the usual one of time and three of space. Because Euclidean universes have no distinct notion of time, they have no structure to put events into a specific order; people living in these universes would not have the words "cause" or "effect" in their vocabulary. Hawking and others taking this approach have said that "time is imaginary," in both a mathematical sense and a colloquial one. Their hope was that causality would emerge as a large-scale property from microscopic quantum fluctuations that individually carry no imprint of a causal structure. But the computer simulations dashed that hope.

WHAT IS CAUSALITY?

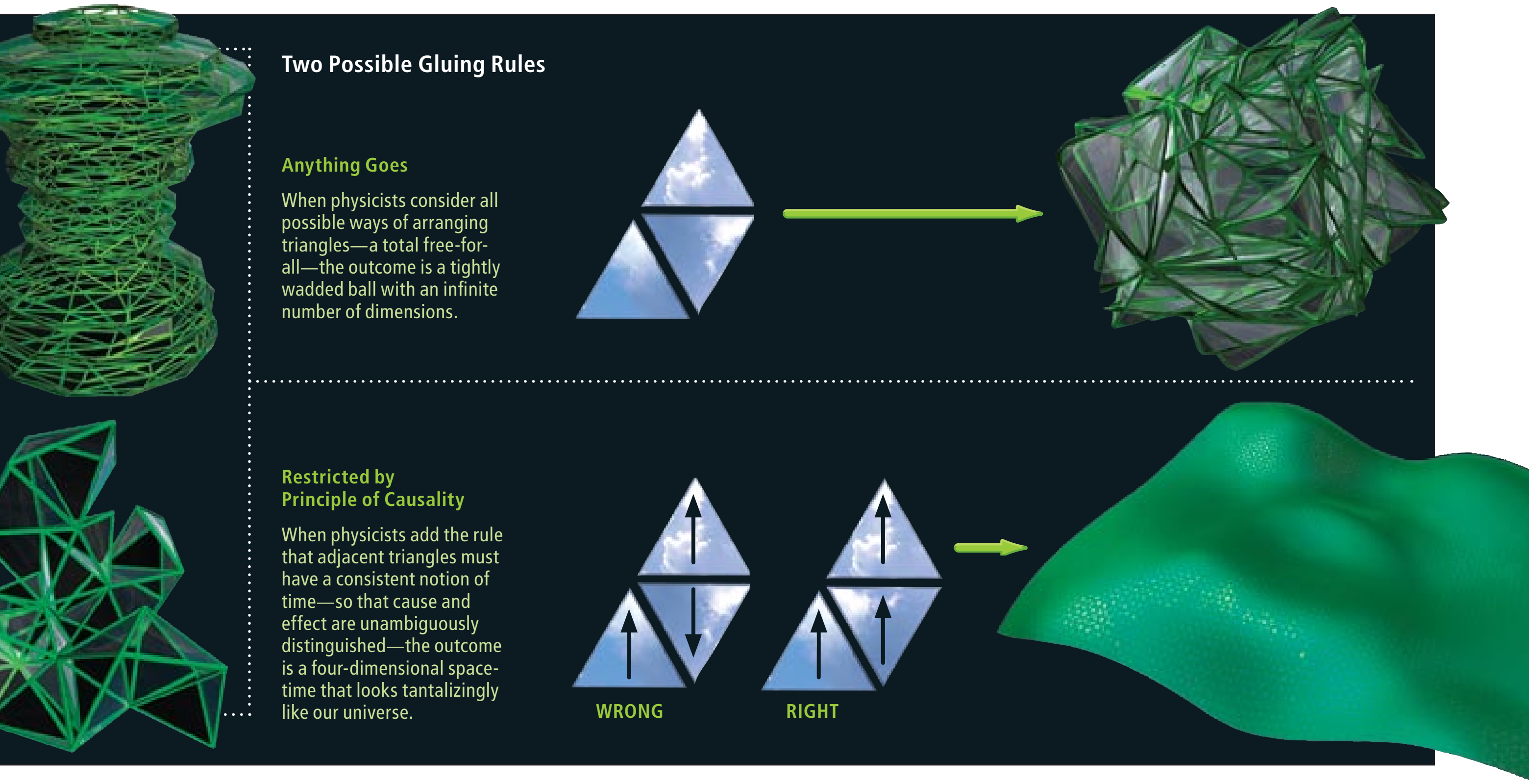
Causality is the principle that events occur in a specific temporal sequence of cause and effect, rather than as a haphazard jumble. In the authors' approach to quantum gravity, the distinction between cause and effect is fundamental to nature, rather than a derived property.



Instead of disregarding causality when assembling individual universes and hoping for it to reappear through the collective wisdom of the superposition, we decided to incorporate the causal structure at a much earlier stage. The technical term for our method is causal dynamical triangulations. In it, we first assign each simplex an arrow of time pointing from the past to the future. Then we enforce causal gluing rules: two simplices must be glued together to keep their arrows pointing in the same direction. The simplices must share a notion of time, which unfolds steadily in the direction of these arrows and never stands still or runs backward. Space keeps its overall form as time advances; it cannot break up into disconnected pieces or create wormholes.

After we formulated this strategy in 1998, we demonstrated in highly simplified models that causal gluing rules lead to a large-scale shape different from that of Euclidean quantum gravity. That was encouraging but not yet the same as showing that these rules are enough to stabilize a full four-dimensional universe. Thus, we held our breath in 2004 when our computer was about to give us the first calculations of a large causal superposition of four-simplices. Did this spacetime really behave on large distances like a four-dimensional, extended object and not like a crumpled ball or polymer?

JEAN-FRANCOIS PODEVIN; IMAGESHOP *Corbis* (dominoes)



Imagine our elation when the number of dimensions came out as four (more precisely, as 4.02 ± 0.1). It was the first time anyone had ever derived the observed number of dimensions from first principles. To this day, putting causality back into quantum-gravitational models is the only known cure for the instabilities of superposed spacetime geometries.

Spacetime at Large

This simulation was the first in an ongoing series of computational experiments whereby we have attempted to extract the physical and geometric properties of quantum spacetime from the computer simulations. Our next step was to study the shape of spacetime over large distances and to verify that it agrees with reality—that is, with the predictions of general relativity. This test is very challenging in nonperturbative models of quantum gravity, which do not presume a particular default shape for spacetime. In fact, it is so difficult that most approaches to quantum gravity—including string theory, except for special cases—are not sufficiently advanced to accomplish it.

It turned out that for our model to work we needed to include from the outset a so-called cosmological constant, an invisible and immaterial substance that space contains even in the complete absence of other forms of matter and energy. This requirement is good news, because cosmologists have found observational evidence for such energy. What is more, the emergent spacetime has what physicists call a de Sitter geometry, which is exactly the solution to Einstein's equations for a universe that contains nothing but the cosmological constant. It is truly remarkable that by assembling microscopic building blocks in an essentially random manner—without regard to any symmetry or preferred geometric structure—we end up with a spacetime that on large scales has the highly symmetric shape of the de Sitter universe.

This dynamical emergence of a four-dimensional universe of essentially the correct physical shape from first principles is the central achievement of our approach. Whether this remarkable outcome can be understood in terms of the interactions of some yet to be identified fundamental "atoms" of spacetime is the subject of ongoing research.

Having convinced ourselves that our quantum-gravity model passed a number of classical tests, it was time to turn to another kind of experiment, one that probes the distinctively quantum structure of spacetime that Einstein's classical theory fails to capture. One of the simulations we have performed is a diffusion process—that is, we let a suitable analogue of an ink drop fall into the superposition of universes

[THE AUTHORS]

Jan Ambjørn, Jerzy Jurkiewicz and Renate Loll developed their approach to quantum gravity in 1998. Ambjørn is a member of the Royal Danish Academy and a professor at the Niels Bohr Institute in Copenhagen and at Utrecht University in the Netherlands. He has a reputation as an accomplished Thai cook, a claim that the editors look forward to evaluating firsthand.

Jurkiewicz is head of the department of the theory of complex systems at the Institute of Physics at the Jagiellonian University in Kraków. His many past positions include one at the Niels Bohr Institute in Copenhagen, along whose shores he was introduced to the beauty of sailing.

Loll is a professor at Utrecht University, where she heads one of the largest groups for quantum gravity research in Europe. Previously she worked at the Max Planck Institute for Gravitational Physics in Golm, Germany, where she held a Heisenberg Fellowship. In her rare spare time, Loll enjoys playing chamber music.

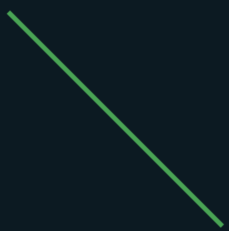
[WHAT IS A DIMENSION, ANYWAY?]

A Whole New Dimension to Space

In everyday life the number of dimensions refers to the minimum number of measurements required to specify the position of an object, such as latitude, longitude and altitude. Implicit in this definition is that space is smooth and obeys the laws of classical physics.

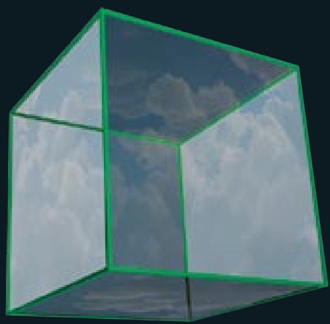
But what if space is not so well behaved? What if its shape is determined by quantum processes in which everyday notions cannot be taken for granted? For these cases, physicists and mathematicians must develop more sophisticated notions of dimensionality. The number of dimensions need not even be an integer, as in the case of fractals—patterns that look the same on all scales.

Integer Dimensions ▼

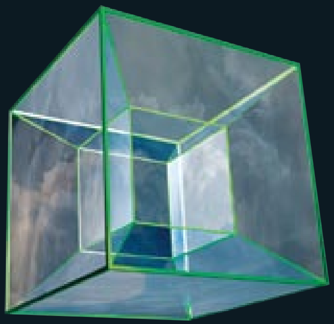


1 Dimension

2 Dimensions

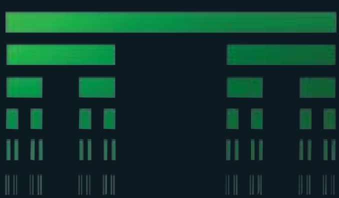


3 Dimensions

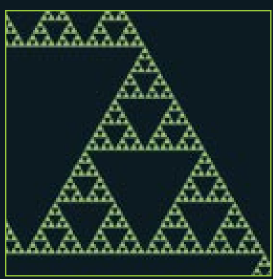


4 Dimensions

Fractal Dimensions ▼



Cantor Set
Take a line, chop out the middle third and repeat ad infinitum. The resulting fractal is larger than a solitary point but smaller than a continuous line. Its Hausdorff dimension [*see below*] is **0.6309**.



Sierpiński Gasket
A triangle from which ever smaller subtriangles have been cut, this figure is intermediate between a one-dimensional line and a 2-D surface. Its Hausdorff dimension is **1.5850**.

Menger Sponge
A cube from which subcubes have been cut, this fractal is a surface that partially spans a volume. Its Hausdorff dimension is **2.7268**, similar to that of the human brain.

Generalized Definitions Of Dimensions

Hausdorff Dimension ▼

Formulated by the early 20th-century German mathematician Felix Hausdorff, this definition is based on how the volume, V, of a region depends on its linear size, r. For ordinary three-dimensional space, V is proportional to r^3. The exponent gives the number of dimensions. "Volume" can also refer to other measures of total size, such as area. For the Sierpiński gasket, V is proportional to $r^{1.5850}$, reflecting the fact that this figure does not even fully cover an area.

Spectral Dimension ▼

This definition describes how things spread through a medium over time, be it an ink drop in a tank of water or a disease in a population. Each molecule of water or individual in the population has a certain number of closest neighbors, which determines the rate at which the ink or disease diffuses. In a three-dimensional medium, a cloud of ink grows in size as time to the $3/2$ power. In the Sierpiński gasket, ink must ooze through a twisty shape, so it spreads more slowly—as time to the 0.6826 power, corresponding to a spectral dimension of 1.3652.

Applying the Definitions

In general, different ways to calculate the number of dimensions give different numbers, because they probe different aspects of the geometry. For some geometric figures, the number of dimensions is not fixed. For instance, diffusion may be a more complicated function than time to a certain power.

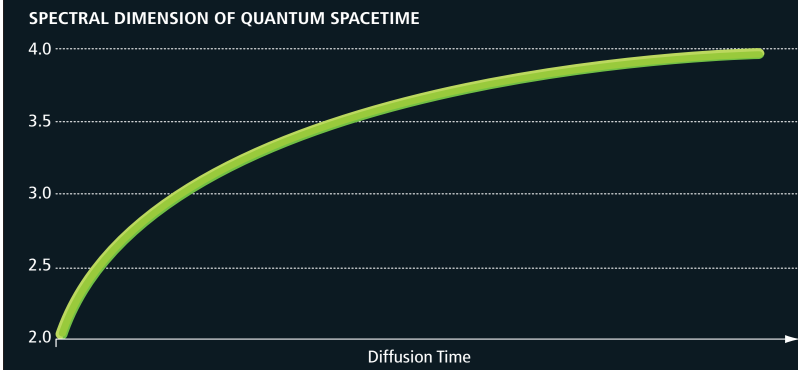
Quantum-gravity simulations focus on the spectral dimension. They imagine dropping a tiny being into one building block in the quantum spacetime. From there the being walks around at random. The total number of spacetime building blocks it touches over a given period reveals the spectral dimension.

JEAN-FRANCOIS PODEVIN

[SIMULATION RESULTS]

Zooming In on Spacetime

By the authors' calculations, the spectral dimension of spacetime shades from four (on large scales) to two (on small scales), and spacetime breaks up from a smooth continuum into a gnarled fractal. Physicists are still puzzling over whether this conclusion means that spacetime ultimately consists of localized "atoms" or is built up out of intricate patterns only very loosely related to our usual concepts of geometry.



Quantum spacetime may be like snow, which is fractal on small scales . . .

. . . but smooth and fully three-dimensional on large ones.

and watch how it spreads and is tossed around by the quantum fluctuations. Measuring the size of the ink cloud after a certain time allows us to determine the number of dimensions in space [*see box on opposite page*].

The outcome is pretty mind-boggling: the number of dimensions depends on the scale. In other words, if we let the diffusion go on for just a short while, spacetime appears to have a different number of dimensions than when we let it run for a long time. Even those of us who specialize in quantum gravity can scarcely imagine how spacetime could smoothly change its dimension depending on the resolution of one's microscope. Evidently, a small object experiences spacetime in a profoundly different way than a large object does. To that object, the universe has something akin to a fractal structure. A fractal is a bizarre kind of space where the concept of size simply does not exist. It is self-similar, which means that it looks the same on all scales. This implies there are no rulers and no other objects of a characteristic size that can serve as a yardstick.

How small is "small"? Down to a size of about 10^{-34} meter, the quantum universe at large is well described by the classical, four-dimensional de Sitter geometry, although quantum fluctuations become increasingly significant. That one can trust the classical approximation to such short distances is rather astonishing. It has important implications for the universe both very early in its history and very far into its future. At both these extremes the universe is effectively empty. Early on, gravitational quantum fluctuations may have been so enormous that matter barely registered; it was a tiny raft tossed on a roiling ocean. Billions of years from now, because of the universe's rapid expansion, matter will be so diluted that it likewise will play little or no role. Our technique may explain the shape of space in both cases.

On still shorter scales, quantum fluctuations of spacetime become so strong that classical, intuitive notions of geometry break down altogether. The number of dimensions drops from the classical four to a value of about two. Nevertheless, as far as we can tell, spacetime is still continuous and does not have any wormholes. It is not as wild as a burbling spacetime foam, as the late physicist John Wheeler and many others imagined. The geometry of spacetime obeys nonstandard and nonclassical rules, but the concept of distance still applies. We are now in the process of probing even finer scales. One possibility is that the universe becomes self-similar and looks the same on all scales below a certain threshold. If so, spacetime does not consist of strings or atoms of spacetime, but a region of infinite boredom: the structure found just below the threshold will simply repeat itself on every smaller scale, ad infinitum.

It is difficult to imagine how physicists could get away with fewer ingredients and technical tools than we have used to create a quantum universe with realistic properties. We still need to perform many tests and experiments—for example, to understand how matter behaves in the universe and how matter in turn influences the universe's overall shape. The holy grail, as with any candidate theory for quantum gravity, is the prediction of observable consequences derived from the microscopic quantum structure. That will be the ultimate criterion for deciding whether our model really is the correct theory of quantum gravity. ■

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Deriving Dimensions. Adrian Cho in *Physical Review Focus;* September 28, 2004. **http://focus.aps.org/story/v14/st13**

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Renate Loll's Web site is **www.phys.uu.nl/~loll**

LUCY READING-IKKANDA; NOAA/PHOTO RESEARCHERS, INC. (*snowflake*); TERRY W. EGGERS *Corbis* (*snowdrift*)

New Jobs *for* Ancient Chaperones

Protective heat shock proteins present in every cell have long been known to counteract stress. Newly recognized roles in cancer and immunity make them potential therapeutic allies

BY PRAMOD K. SRIVASTAVA

KEY CONCEPTS

- Guardian proteins, found in all forms of life, keep a wide variety of cellular processes running smoothly.
- Through their diverse interactions, these proteins pick up telltale "fingerprints" of each cell's contents, which has allowed them to evolve a critical role in immune responses to cancer or pathogens.
- Therapies that take advantage of these proteins include inhibitors and enhancers of their various natural functions.

—The Editors

In 1962 someone at the Genetics Institute in Pavia, Italy, turned up the temperature in an incubator holding fruit flies. When Ferruccio Ritossa, then a young geneticist, examined the cells of these "heat shocked" flies, he noticed that their chromosomes had puffed up at discrete locations. The puffy appearance was a known sign that genes were being activated in those regions to give rise to their encoded proteins, so those sites of activity became known as the heat shock loci.

The effect was reproducible but initially considered to be unique to the fruit fly. It took another 15 years before the proteins generated when these chromosome puffs appear were detected in mammals and other forms of life. In what is certainly among the most absorbing stories in contemporary biology, heat shock proteins (HSPs) have since been recognized as occupying a central role in *all* life—not just at the level of cells but of organisms and whole populations.

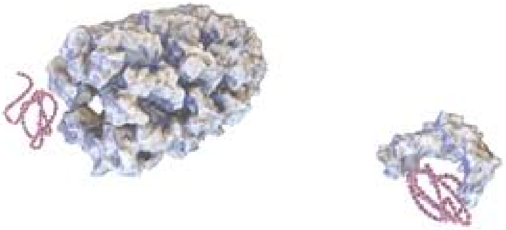
Indeed, these ubiquitous molecules are among the most ancient survival mechanisms to have been conserved throughout evolution. They have even been shown to facilitate evolution itself. Produced in response to stressful conditions, including (but not limited to) heat, HSPs help individual cells to cope by keeping cellular processes working smoothly in the face of adversity. In the past decade scientists have realized that HSPs also play additional roles in higher organisms, such as humans. They are integral to our immune defenses against cancer and pathogens and might therefore prove valuable in developing a wide variety of new medicines and vaccines.

To understand how these versatile proteins can be harnessed therapeutically, it is helpful to look at the diverse ways they perform their core job, which is to act as "chaperones" for other proteins. Like the chaperoning of people, the work of HSPs has two objectives: to inhibit undesirable interactions and to promote desirable ones, so that a stable and productive bond forms between protein partners.

Versatile Escorts

Proteins inside a cell often have just one or a very few correct "mates" with which they can interact effectively—for example, a receptor and its ligand, which behave like a lock and key, respectively. The ligand has little effect on other receptor types, and the receptor is typically activated only by its particular ligand or molecules very close to it in structure. In contrast, HSPs tend to associate with a wide range of "client" proteins, allowing the HSPs to perform a dizzying array of jobs. These can include helping newly formed amino acid chains to fold into their proper protein shapes, dismantling them after they have been damaged, escorting proteins to their intended mates and keeping them away from interlopers.

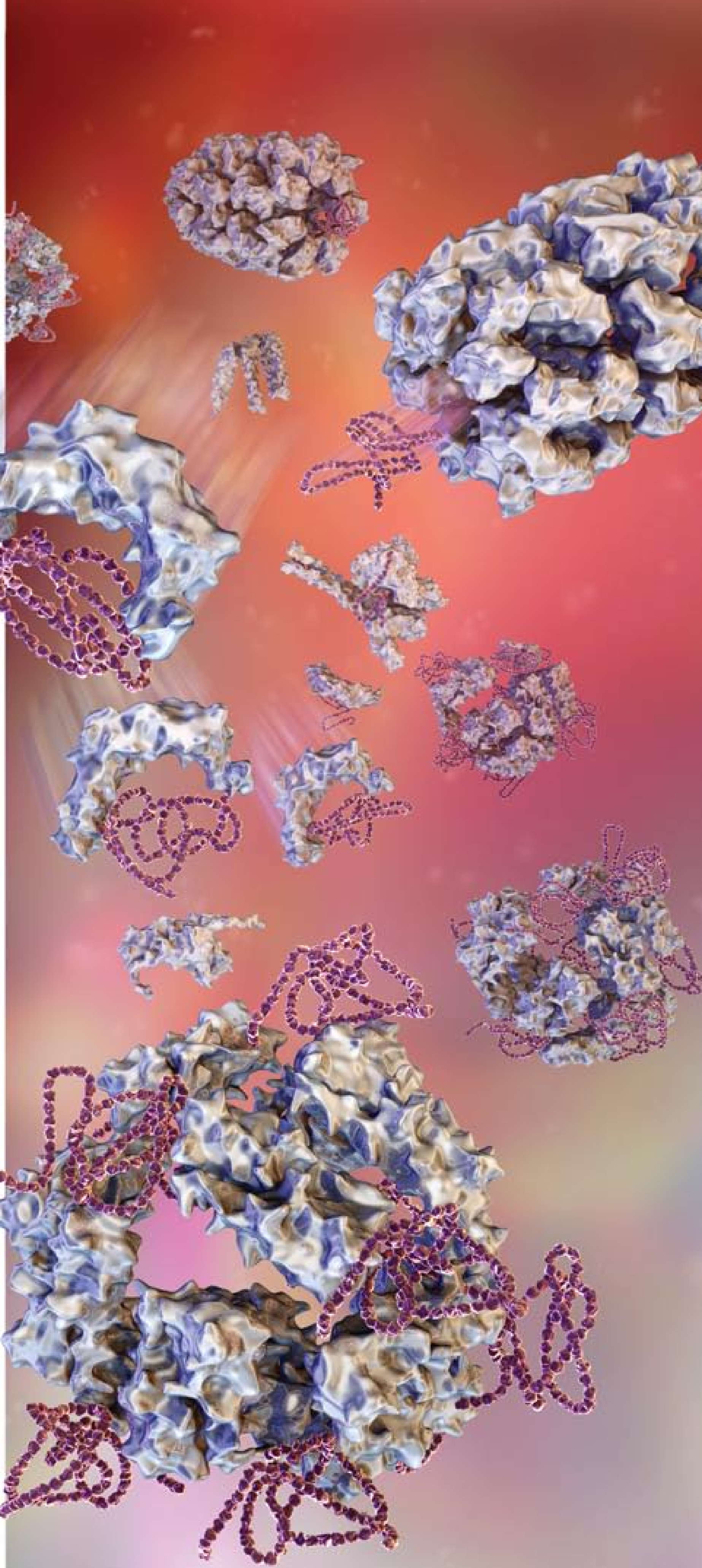
Specific examples can highlight just how critical these tasks are and can illustrate some of the



ways that major HSP chaperones serve their clients. A protein's ability to carry out its intended functions depends not only on it getting to the right place at the right time, but on it having the correct shape. Newly formed chains of amino acids are subject to various forces that help them to take on the right conformation. Each amino acid, for instance, has a characteristic response to water in the cellular cytoplasm. Hydrophobic amino acids abhor water and try to get away from it by nestling inside the protein structure, whereas hydrophilic amino acids prefer to face outward. Such mechanisms are not always enough to ensure proper folding, though, so HSPs, such as HSP60, get involved [*see box on page 53*].

Arthur L. Horwich of Yale University has provided much of the current understanding of the HSP60 chaperone, which resembles a cage composed of multiple HSP60 molecules. Its inner rim is highly hydrophobic and therefore attracts the exposed hydrophobic amino acids of an unfolded protein to bind to it. Once such a chain is drawn into this cage, it encounters a hydrophilic interior, which the hydrophobic amino acids want to avoid at all costs, so the trapped molecule is forced to change shape. This process may not happen in one go, and the cage may release and recapture the protein multiple times before the protein acquires a correctly folded conformation. Thus, the HSP60 protein is known as a foldase. Conversely, the HSP100 protein is an unfoldase. It, too, is a multisubunit ring, which, in cooperation with HSP70, can disassemble damaged proteins or undesirable protein aggregates or can even cause a fully folded protein to unfold.

In contrast to the cagelike chaperones, most HSPs do not enclose their substrates but rather grab them by the "elbows" to help them along. HSP70, for example, binds directly to short stretches of amino acid sequences, also known as peptides. The molecule has a peptide-binding



JEFF JOHNSON *Hybrid Medical Animation*

HEAT SHOCK PROTEINS are cellular chaperones, protecting the integrity of proteins by helping them to take and keep the proper shape, to get to the right places and to avoid unwanted interactions.

cleft that is open when HSP70 is bound to the cellular energy source ATP, but when ATP is absent, a lidlike structure on HSP70 clamps down on the bound peptide and traps the larger protein chain in place. The ability of HSP70 to grab a variety of different peptides allows the molecule to play chaperone in many fundamental cellular processes, such as helping new amino acid chains to assume a mature conformation, facilitating the assembly of complex proteins and protecting proteins from falling apart in high temperatures.

Although heat shock proteins are active in cells in normal circumstances, it is easy to see how their help would be even more valuable to a cell in a difficult situation. Under emergency conditions, such as extreme heat or cold, oxygen deprivation, dehydration or starvation, a cell would be struggling just to survive. Critical proteins might be degraded by the harsh environment, even as the cell would try to churn out replacements. In these circumstances, heat shock proteins would mitigate the stress by rescuing essential proteins, dismantling and recycling damaged ones, and generally keeping cell operations running as smoothly as possible. Hence, when a cell is under high stress, one of its first responses will be to manufacture more of the HSPs themselves, as Ritossa first witnessed 46 years ago. This important role of HSPs has been well documented since its discovery [see "How Cells Respond to Stress," by William J. Welch; Scientific American, May 1993]. Beginning in the 1980s, however, a completely different function of HSPs—just as integral to survival for complex organisms—also began to be revealed.

Antigenic Fingerprints

As a graduate student in the early 1980s at the Center for Cellular and Molecular Biology in Hyderabad, India, I became interested in a phenomenon that had been observed since the 1940s but never explained. Many scientists had demonstrated that one can immunize rodents against their own cancers, just as people are routinely immunized against pathogens. Proteins from a pathogen are recognized by the mammalian immune system as foreign, however, and that is why they act as antigens—provoking an immune response. A cancer, on the other hand, is made up of an individual's own cells, so the antigenic element remained a great mystery. I began trying to isolate these cancer-specific antigens.

During my graduate and postdoctoral work, I identified a protein, called gp96, which could indeed elicit immune resistance to tumors. This molecule, surprisingly, turned out to be a member of the HSP90 family—many HSP proteins come in several related forms—which occurs in normal tissues as well as cancer cells. Stephen J. Ullrich and his colleagues at the National Institutes of Health independently made a similar observation two years later. The gp96 molecules found in tumors and in normal tissues were identical in their amino acid sequences, so the cancer-derived gp96 was not cancer-specific. What, then, was the basis of its ability to immunize against cancers?

The answer began to emerge in 1990, when Heiichiro Udono, then a postdoctoral fellow in my laboratory at the Mount Sinai School of Medicine, and I were isolating HSP70 from tumors to test if it, too, elicited tumor immunity. We found that it could. The biggest surprise came, however, when we put the HSP70 through a final purification step called ATP-affinity chromatography, and the molecule's very potent tumor-immunizing activity disappeared!

We realized immediately that exposure of HSP70 to ATP was causing HSP70 to shed material, which we determined to be peptides. The work of several research groups in the ensuing years has revealed that HSP70 changes conformation when it binds to ATP, causing it to let go of any bound peptide. In fact, researchers learned that members of the HSP60, HSP70 and HSP90 families all regularly carry around peptides generated within cells. And when HSP70 or HSP90 are taken from cancers or from virus- or tuberculosis-infected cells, in nearly all instances they bear peptides derived from cancer-specific antigens, viral antigens or tuberculosis antigens. Thus, the HSP-associated peptides represent the "antigenic fingerprint" of the cells or tissues from which they come.

This characteristic ability of certain chaperones to retain peptides representative of their cell of origin has given HSPs an essential role in one of the most fundamental processes of the immune system—recognition of cancerous and virus-infected cells. T lymphocytes recognize antigens on such cells through an elaborate process known as antigen presentation. Essentially all antigens made inside cells are degraded into peptides that then associate with HSPs of the HSP60, HSP70 and HSP90 families in a sequence of events that is still unclear. The peptides are eventually loaded onto a special class of proteins, known as the major histocompatibility complex I (MHC I) proteins, displayed on the surface of most mam-

STRESS RESPONSE

Chromosomes of a fruit fly exposed to high heat appear to "puff up" in regions containing genes that encode heat shock proteins (*white* and *green*). For a cell to manufacture those proteins, the tightly coiled DNA must unravel slightly so that the relevant genes are accessible, leading to the puffy appearance at those locations.

[THE AUTHOR]

Pramod K. Srivastava is a professor of medicine and director of the Center for Immunotherapy of Cancer and Infectious Diseases at the University of Connecticut School of Medicine. In a series of discoveries beginning when he was a graduate student, Srivastava pioneered the study of the role of heat shock proteins in the immune system. Based on those insights, he co-founded the company Antigenics to develop cancer vaccines made with HSPs derived from individual patients' tumors. He remains a consultant to the company and continues to investigate the role of HSPs in immune responses.

COURTESY OF PRAMOD K. SRIVASTAVA (*Srivastava*); COURTESY OF J. WERNER AND J. T. LIS IN *SCIENCE*, VOL. 301; AUGUST 2003 (*chromosomes*) malian cells. The T cells recognize these MHC I–peptide complexes and destroy any that signify the cell is diseased [*see box on next page*].

The chaperoning of peptides by HSPs is essential for their eventual loading onto MHC I molecules; when the HSPs are chemically silenced, the MHC I molecules remain empty of peptides and cannot be recognized by the T cells. This role of the HSP-chaperoned peptides in antigen presentation by MHC molecules was hypothesized by my colleagues and me in 1994 and shown to be true through our work and others'.

It is this antigen-chaperoning property of the peptide-binding HSPs that is the basis of the ability of HSPs derived from tumors or pathogen-infected cells to immunize against those same tumors or intracellular pathogens. But the HSP-peptide complexes also have another critical part in the T cells' recognition of friend and foe antigens—through their interactions with different types of immune cells known as antigen-presenting cells.

Sounding the Alarm

Sentinels of the immune system, antigen-presenting cells occur in perhaps every tissue of the body, where they can "sample" their surroundings for any antigens that might be nearby. They present whatever they encounter to the T cells that will eventually home in on and attempt to destroy cancerous or infected cells.

It turns out that antigen-presenting cells carry receptors on their surface for the peptide-binding chaperones. The first such receptor was identified by Robert J. Binder, then a graduate student in my laboratory and currently an assistant professor at the University of Pittsburgh, as CD91. When the cells encounter an HSP-peptide complex, they internalize it through the CD91 doorway and present the HSP-chaperoned peptides to the T cells, which can then multiply and fight off the cancer or pathogen. Broadly speaking, this mechanism is the reason HSPs isolated from a cancer are able to immunize against that cancer, whereas the HSPs isolated from normal tissues do not do so.

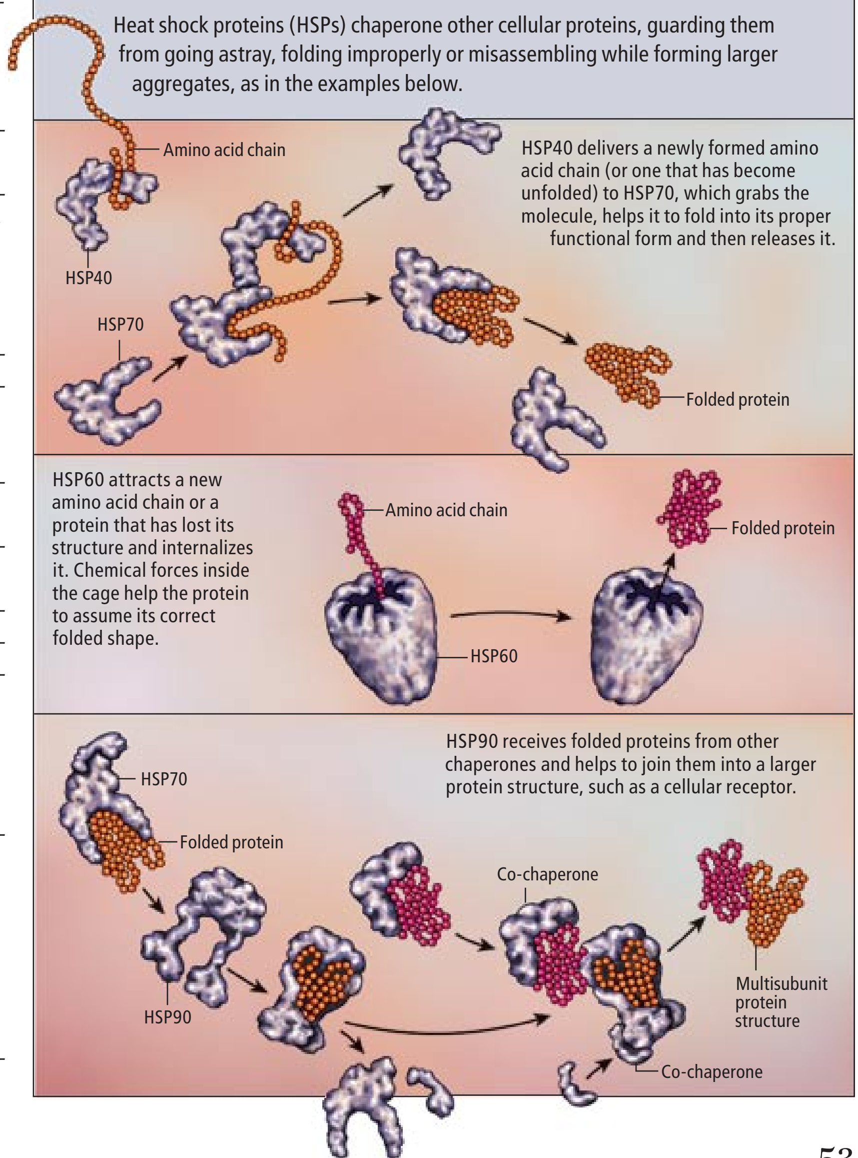
Beyond delivering a description of the invader to the immune system, HSPs seem to sound an alarm as well. Sreyashi Basu of the University of Connecticut School of Medicine and I have shown in laboratory studies that just exposing antigen-presenting cells to HSP70 and HSP90 family members causes the cells to undergo a number of changes, including initiation of signals that cause inflammation, which is part of a strong immune defense. Although HSPs normally do their work inside cells, scientists have known for some time that when mammalian cells are under stress, selected HSPs are released from the cells or displayed on the cell surface in small but significant quantities. Thus, the ability of HSPs to activate antigen-presenting cells by their mere presence suggests that an anomalous appearance of HSPs outside cells may be a mechanism to alert the immune system of danger.

My work toward using HSP-peptide complexes purified from cancers to elicit tumor rejection is based on this immunizing function and on my belief that each patient's tumor is antigenically unique. I have developed a process for extracting HSP-bound peptides from the individual patient and then reintroducing them in purified form as

[PRIMARY ROLE]

KEEPING ORDER

Heat shock proteins (HSPs) chaperone other cellular proteins, guarding them from going astray, folding improperly or misassembling while forming larger aggregates, as in the examples below.

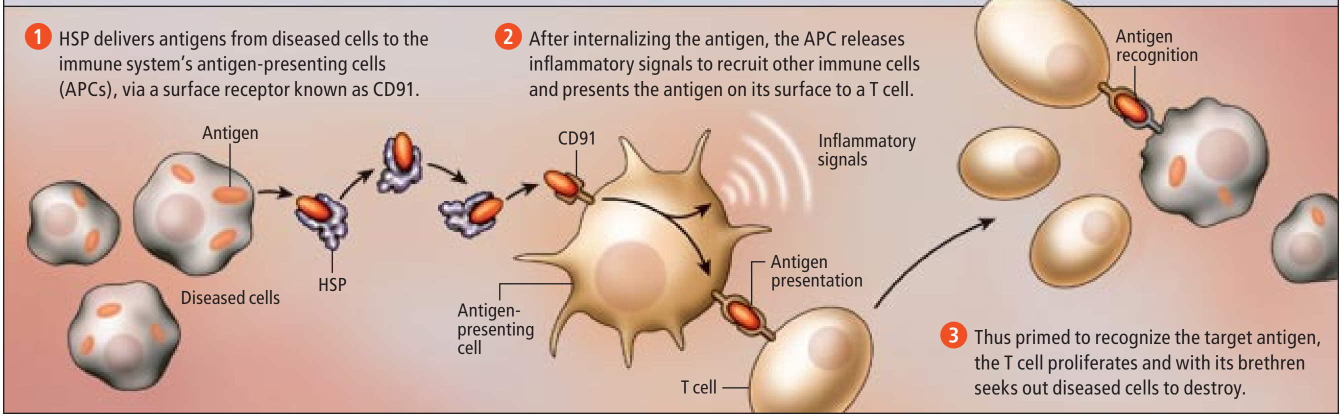


JEN CHRISTIANSEN

[A SECOND JOB]

ACTIVATING IMMUNE RESPONSES

When a cell is cancerous or infected by a pathogen, it generates proteins not found in normal cells. Fragments of such proteins can then potentially act as antigens, substances that provoke an immune response. But immune cells must first be made aware of the problem. Heat shock proteins, primarily members of the HSP90 and HSP70 families, participate in sounding the alarm and identifying the culprits.



a vaccine that would stimulate the immune system to attack cells bearing those specific tumor-associated antigens. This approach has been tested in the U.S. and Europe in a series of early human (phase I and II) trials for several cancers. More advanced tests of efficacy (randomized phase III trials) in the U.S., Europe, Australia and Russia have just been concluded in patients with melanoma and renal cancer. Those latest studies showed that patients with melanoma who received sufficient doses of HSP-peptide-complex vaccine and whose disease was limited to the skin, lymph nodes and lungs lived significantly longer than patients who received other standard treatments, including chemotherapy. In the trial on renal cancers, the vaccine extended the recurrence-free survival time in some groups of patients by more than a year and a half.

The results were enough for the Russian government to approve the treatment, making it the first cancer vaccine to enter actual clinical use. An application for approval in Europe will be filed shortly, and an application to the U.S. Food and Drug Administration is awaiting more data on the patients' long-term outcomes. Meanwhile this approach seems as if it should be just as applicable for treatment of serious infectious diseases, including genital herpes, tuberculosis and others. Clinical trials investigating those applications are at various stages.

Wide Influence

Amplifying the natural effect of HSPs on the immune system by using them in vaccines is not the only way to employ these versatile proteins therapeutically. Work by Suzanne L. Rutherford of the University of Washington and Susan L. Lindquist of the Whitehead Institute for Biomedical Research in Cambridge, Mass., has provided a stunning example of how effectively HSPs perform their core job of mitigating stressful conditions inside cells. They have shown that when HSP90 functioning was suppressed in fruit flies, a large number of preexisting genetic mutations were unmasked, indicating that potentially deleterious effects were being buffered by HSP90. Rutherford and Lindquist have argued that widespread genetic variation that would otherwise affect the functioning of organisms exists in nature but is usually not manifested because HSP90 essentially hides the variation—an effect that fosters the quiet accumulation of genetic changes. When the buffering function is compromised, for example, by extreme temperature, variant traits emerge and then natural selection can act on them. Thus, HSP90, by fostering genetic variation, potentiates evolution.

Lindquist and her collaborators have provided further evidence of a role for HSP90 in the rapid evolution of novel traits, such as resistance to specific drugs, in diverse species of fungi. As a result, she has suggested that species-specific inhibitors of HSP90 may be used as a new generation of antibiotics. Similarly, HSPs are believed to provide buffering against the accumulating mutations that should make cancer cells less and less viable but instead seem to drive their malignancy. Because HSP90 affects a wider variety of intracellular signaling pathways than any other HSP does, loss of its function should make cancer cells more sensitive to stress and therefore more easily killed by chemotherapy.

BENEFICIAL STRESS

Exercise raises body temperature and generates other forms of stress on cells throughout the body, causing them to increase their manufacture of certain heat shock proteins. Preliminary research suggests that these HSPs might contribute to the health benefits of exercise by mitigating damage inside cells and by alerting the immune system to boost overall immune responses.

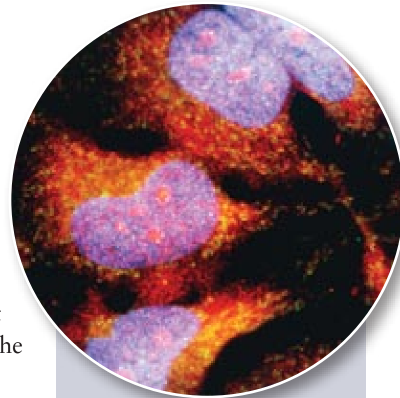
JEN CHRISTIANSEN (*illustration*); ANTHONY WEST *Corbis* (*runner*)

Hence, pharmacological inhibitors of increasing specificity for HSP90 are being tested in cancer patients, in combination with chemotherapy.

While I was testing the efficacy of HSP-peptide complexes in cancer immunotherapy, I noticed the seemingly strange phenomenon that immunization with very high doses of HSPs did not elicit immunity but rather caused suppression of immune responses. These studies, carried out with Rajiv Chandawarkar of the University of Connecticut Health Center, showed that HSPs could act not only as immunostimulators but also as immunosuppressants. In studies of mice, we showed that high doses could suppress autoimmune type 1 diabetes and encephalitis. Irun R. Cohen of the Weizmann Institute of Science in Rehovot, Israel, and his collaborators have long pursued the idea that HSP60 and one of its peptides are autoantigens in human type 1 diabetes, triggering an immune attack on the body's insulin-producing cells. In clinical trials they have demonstrated some value in blocking the peptide, and further tests in humans are under way.

Although the diverse roles of HSPs make them attractive agents for treating a variety of diseases, their very universality raises a danger: drugs aiming to alter HSP levels run the risk of harming many body systems that rely on the proteins. Nevertheless, the history of drug development is replete with examples of scientists having learned to modulate essential proteins without causing unacceptable side effects, and HSPs are certain to be at the center of a growing list of applications in the fullness of time.

From a wider perspective, these primitive, abundant molecules have been maintained since the very dawn of life because they were needed for the basic infrastructure of life as we know it—to help bring proteins into being, to help degrade them, to protect fragile proteins from the abundant stresses of the primordial environment and to protect cells from the disruptive effects of mutations. As newer biological functions emerged, such as immunity, the evolutionary process made use of what was already plentiful by employing HSPs in antigen presentation. I doubt that we are close to having fully plumbed the depths of the activities of these magical molecules. As further insights into the workings of life are gained, previously unimagined roles for the diligent chaperones are likely to be revealed. ■



HARMFUL HELPERS

Cancer cells, because they are abnormal, are under stress most of the time, generating higher levels of heat shock proteins as a result. HSP90 (*yellow, above*) in particular is believed to help cancer cells survive the stressful conditions, just as it does for normal cells. Inhibiting HSP90's effect could make malignant cells more vulnerable to toxic therapies.

NANCY KEDERSHA *Photo Researchers, Inc. (micrograph)*

NOW IN TRIALS

A number of drugs currently in clinical trials would fight disease by taking advantage of the diverse functions of heat shock proteins. Some seek to inhibit the proteins, others to induce them, depending on the disorder and the HSP that is being employed or targeted.

TREATMENT MECHANISM

🔴 **Inhibitor of HSPs**
(compound able to block the functioning of HSPs that would normally help a cancer cell, virus-infected cell or pathogenic bacterium to survive)

🟢 **Induction of HSPs**
(heat or chemicals able to induce a patient's own HSPs to protect an organ during surgical or other treatments)

🔵 **Vaccine/Immunotherapy**
(antigenic HSP-peptide complexes that are purified, then introduced into the body to stimulate an immune response to a tumor or pathogen)

**Approved for clinical use in Russia*

HSP	TREATMENT (MANUFACTURER)	DISORDER
HSP90	🔴 Alvespimycin (Kosan Biosciences)	Breast cancer
	🔴 Tanespimycin (Kosan Biosciences)	Leukemia, lymphoma, solid tumors
	🔴 CNF 2024 (Biogen Idec)	
	🔴 SNX-5422 mesylate (Serenex)	
	🔴 AUY-922 (Novartis)	Solid tumors
	🔴 IPI-504 (Infinity Pharmaceuticals)	Melanoma, prostate cancer
	🔴 BIIB021 (Biogen Idec)	Leukemia, lymphoma, solid tumors
HSP27	🔴 OGX-427 (OncoGenex Technologies)	Solid tumors
Various	🟢 Radio-frequency therapy	Melanoma
HSP65	🔵 HspE7 (Nventa Biopharmaceuticals)	Precancerous cervical cells infected with human papillomavirus
HSP70	🔵 AG-707 (Antigenics)	Herpes simplex type 2
	🔵 HSPPC-70/AG-858 (Antigenics)	Chronic myeloid leukemia
Gp96	🔵 HSPPC-96/vitespen* (Antigenics)	Solid tumors

➡ MORE TO EXPLORE

Roles of Heat-Shock Proteins in Innate and Adaptive Immunity. Pramod K. Srivastava in *Nature Reviews Immunology*, Vol. 2, No. 3, pages 185–194; March 2002.

HSP90 and the Chaperoning of Cancer. Luke Whitesell and Susan L. Lindquist in *Nature Reviews Cancer*, Vol. 5, No. 10, pages 761–772; October 2005.

Heat Shock Factor 1 Is a Powerful Multifaceted Modifier of Carcinogenesis. Chengkai Dai et al. in *Cell*, Vol. 130, No. 6, pages 1005–1018; September 21, 2007.

Phase III Comparison of Vitespen, an Autologous Tumor-Derived Heat Shock Protein gp96 Peptide Complex Vaccine, with Physician's Choice of Treatment for Stage IV Melanoma: The C-100-21 Study Group. Alessandro Testori et al. in *Journal of Clinical Oncology*, Vol. 26, No. 6, pages 955–962; February 20, 2008.

Traces of a DISTANT PAST

DNA furnishes an ever clearer picture of the multimillennial trek from Africa all the way to the tip of South America

BY GARY STIX

A development company controlled by Osama bin Laden's half brother revealed last year that it wants to build a bridge that will span the Bab el Mandeb, the outlet of the Red Sea to the Indian Ocean. If this ambitious project is ever realized, the throngs of African pilgrims who traverse one of the longest bridges in the world on a journey to Mecca would pass hundreds of feet above the probable route of the most memorable journey in human history. Fifty or sixty thousand years ago a small band of Africans—a few hundred or even several thousand—crossed the strait in tiny boats, never to return.

The reason they left their homeland in eastern Africa is not completely understood. Perhaps the climate changed, or once abundant shellfish stocks vanished. But some things are fairly certain. Those first trekkers out of Africa brought with them the physical and behavioral traits—the large brains and the capacity for language—that characterize fully modern humans. From their bivouac on the Asian continent in what is now Yemen, they set out on a decamillennial journey that spanned continents and land bridges and reached all the way to Tierra del Fuego, at the bottom of South America.

Scientists, of course, have gained insight into these wanderings because of the fossilized bones or spearheads laboriously uncovered and stored in collections. But ancestral hand-me-downs are often too scant to provide a complete picture of this remote history. In the past 20 years population geneticists have begun to fill in gaps in the paleoanthropological record by fashioning a genetic bread-crumb trail of the earliest migrations by modern humans.

Almost all our DNA—99.9 percent of the three billion "letters," or nucleotides, that make up the human genome—is the same from person to person. But interwoven in that last 0.1 percent are telltale differences. A comparison among, say, East Africans and Native Americans can yield vital clues to human ancestry and to the inexorable progression of colonizations from continent to continent. Until recent years, DNA passed down only from fathers to sons or from mothers to their children has served as the equivalent of fossilized footprints for geneticists. The newest research lets scientists adjust their focus, widening the field of view beyond a few isolated stretches of DNA to inspect hundreds of thousands of nucleotides scattered throughout the whole genome.

Scanning broadly has produced global migratory maps of unprecedented resolution, some of which have been published only during recent months. The research provides an endorsement of modern human origins in Africa and shows how that continent served as a reservoir of genetic diversity that trickled out to the rest of the world. A genetic family tree that begins with the San people of Africa at its root ends with South American Indians and Pacific Islanders on its youngest-growing branches.

The study of human genetic variation—a kind of historical Global Positioning System—goes back to World War I, when two physicians work-

KEY CONCEPTS

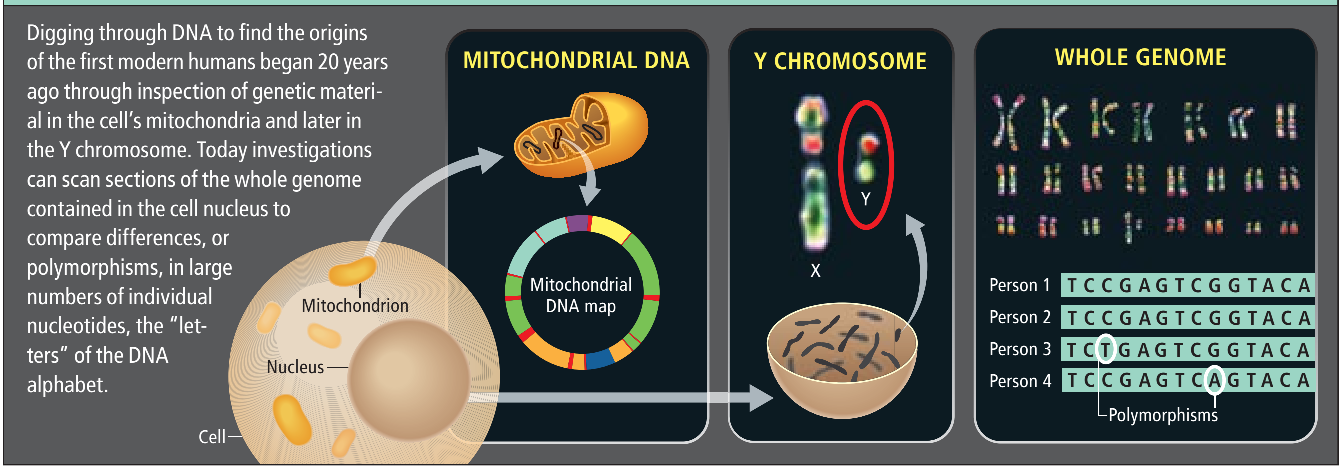
- Scientists trace the path of human migrations by using bones, artifacts and DNA. Ancient objects, however, are hard to find.
- DNA from contemporary humans can be compared to determine how long an indigenous population has lived in a region.
- The latest studies survey swathes of entire genomes and produce maps of human movements across much of the world. They also describe how people's genes have adapted to changes in diet, climate and disease.

—The Editors

ILLUSTRATION BY SEAN McCABE; SOURCES: DANIEL SAMBRAUS (*human skull*), PASCAL GOETGHELUCK (*Neandertal skull*), BIOPHOTO ASSOCIATES (*chromosomes*) *Photo Researchers, Inc.*

[METHODS]

GENETIC PROSPECTING



Digging through DNA to find the origins of the first modern humans began 20 years ago through inspection of genetic material in the cell's mitochondria and later in the Y chromosome. Today investigations can scan sections of the whole genome contained in the cell nucleus to compare differences, or polymorphisms, in large numbers of individual nucleotides, the "letters" of the DNA alphabet.

ing in the Greek city of Thessaloníki found that soldiers garrisoned there had a differing incidence of a given blood group depending on their nationality. Beginning in the 1950s, Luigi Luca Cavalli-Sforza started formalizing the study of genetic differences among populations by examining distinct blood group proteins. Variations in proteins reflect differences in the genes that encode them.

Then, in 1987, Rebecca L. Cann and Allan C. Wilson of the University of California, Berkeley, published a groundbreaking paper based on analyzing the DNA of mitochondria, the cell's energy-producing organelles, which are passed down through the maternal line. They reported that humans from different populations all descended from a single female in Africa who lived about 200,000 years ago—a finding that immediately made headlines trumpeting the discovery of the "Mitochondrial Eve." (Despite the Biblical allusion, this Eve was not the first woman: her lineage, though, is all that has survived.)

All about Eve

The fast, relatively predictable rate of "neutral" mitochondrial mutations—ones that are neither beneficial nor harmful—lets the organelles operate as molecular clocks. Counting the differences in the number of mutations (ticks of the clock) between two groups, or lineages, allows a researcher to construct a genetic tree that tracks back to a common ancestor—Mitochondrial Eve or another woman who founded a new lineage. Comparison of the ages of the lineages from different regions permits the building of a timeline of human migrations.

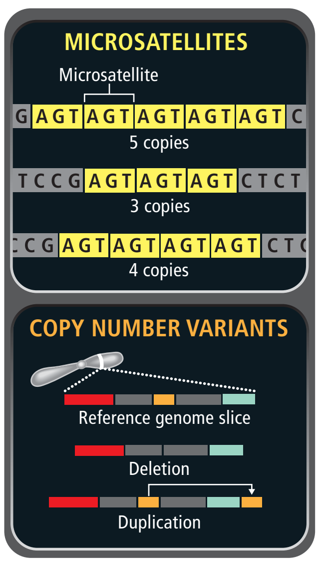
Since 1987 the data bank on human diversity has broadened to encompass the Y chromosome—the sex chromosome passed down only by males to their sons. The male-transmitted DNA carries many more nucleotides than mitochondrial DNA does (tens of millions, as opposed to just 16,000), enhancing investigators' ability to distinguish one population from another. Analyzing mitochondrial and Y chromosome DNA from human populations has turned up hundreds of genetic markers (DNA sites having identifiable mutations specific to particular lineages).

The route humans took from Africa to the Americas over the course of tens of thousands of years can now be tracked on the map as if the travelers were moving, albeit extremely slowly, on a series of interconnected superhighways. Alphanumeric route signs, such as I-95, can be recast as alphanumeric genetic markers. In the case of the Y chromosome, for instance, cross the Bab el Mandeb on highway (genetic marker) M168, which becomes M89 when heading north through the Arabian Peninsula. Make a right at M9 and set out toward Mesopotamia and beyond. Once reaching an area north of the Hindu Kush, turn left onto M45. In Siberia, go right and follow M242 until it eventually traverses the land bridge to Alaska. Pick up M3 and proceed to South America [*see map on opposite page*].

Mitochondrial DNA and the Y chromosome remain powerful analytical instruments. The National Geographic Society, IBM and the Waitt Family Foundation have joined in a privately funded $40-million collaboration through 2010, research that is primarily devoted to using these tools. With the help of 10 regional academic institutions, the so-called Genographic Project is gathering DNA from up to 100,000 indigenous people worldwide. "What we're focusing on is the details of how people made the jour-

MANY WAYS TO SLICE A GENOME

Scientists continually seek genetic markers—characteristic patterns of nucleotides—that differ from one population group to another and that can be used when comparing whole genomes. Microsatellites, short repetitive nucleotide segments found on all the chromosomes (*top*), have served as markers for a number of years. A new type of whole-genome analysis looks for what are called copy number variants—deletions or duplications of up to one million nucleotides (*bottom*).



JEN CHRISTIANSEN; CNRI/PHOTO RESEARCHERS, INC. (*chromosome images*) neys," says Spencer Wells, who heads the project. In a recent report its researchers found that the Khoisan people of southern Africa remained genetically separate from other Africans for 100,000 years. In another study, they demonstrated that some of the gene pool of Lebanese men can be traced to Christian Crusaders and Muslims from the Arabian Peninsula.

Power Tools

Genetic researchers have sampled the DNA of many people living along the migratory routes they have discovered. Yet the seeming certainty of the data sometimes deceives. Scientists who study human origins still would prefer a fossil they can hold in their hands over a genealogical tree. DNA differs from the radioactive isotopes used to date fossils. The rate of mutation can fluctuate from one stretch of DNA to another.

But paleoanthropologists are in a fix. Fossil remains are rare and too often incomplete. The earliest migration from Africa to Australia shows up in mitochondrial and Y genetic material (thanks to Andaman Islanders, among others), but the physical artifacts are largely missing along the route.

HITCHHIKING

Microorganisms that ride in or on people can help researchers confirm discoveries about human migrations. The genes of *Helicobacter pylori* (*above*), the ulcer-causing bacterium endemic to humans, indicate that the microbe left Africa about 55,000 years ago, just when humans did. One lineage of the microbe appears both in East Asian and in native South American populations, supporting the notion that South Americans originally came from Asia.

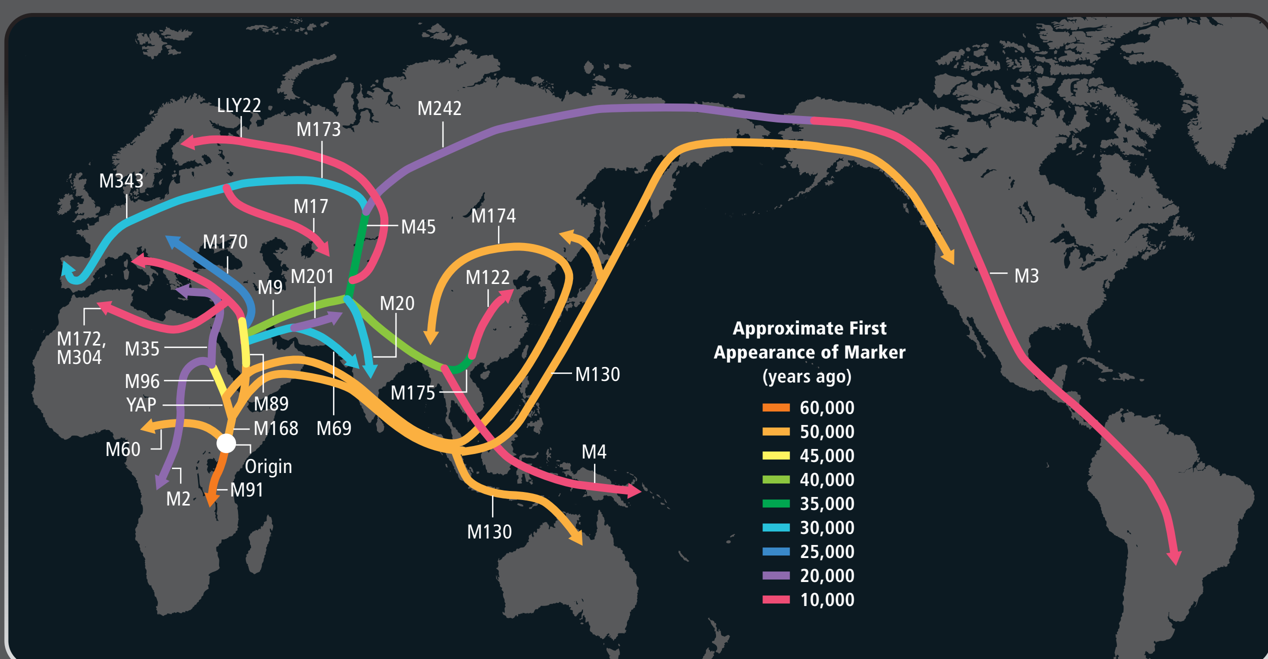
The answer to the absence of stones and bones: more DNA, from wherever. To bolster the case for genetics, researchers have looked to microbes that have hitched a ride on humans, inspecting their genes to look for similar patterns of migration. Freeloaders include bacteria, viruses and even lice. Besides microorganisms, the Human Genome Project and related efforts to look across the expanse of whole genomes have yielded a set of power tools that are helping to compensate for deficiencies in genetic methods. "You can look at so many different places in the genome from many individuals and in many populations to achieve more statistical power in testing different hypotheses," says Tim Weaver, a professor of anthropology at the University of California, Davis.

During this decade, researchers have made dramatic discoveries by simultaneously comparing a multitude of variable, or polymorphic, sites interspersed throughout the genome's three billion nucleotides. The first whole-genome studies earlier in this decade looked at differences among populations in short repetitive stretches of DNA known as microsatellites. More recently, the scope afforded by whole-genome scans

[ROUTE MAPS]

TRACKING Y CHROMOSOMES THROUGH TIME

Geneticists can track the path of ancient migrations by examining genetic markers in Y chromosomes from men who hail from different parts of the world. Each marker, such as M168 or M89, identifies a lineage of men and where the lineage originated. By building an evolutionary tree based on observing many living people with the markers, investigators can determine the approximate ages of the lineages.



JEN CHRISTIANSEN; INFORMATION SOURCE: NATIONAL GEOGRAPHIC MAPS; P. HAWTIN *Photo Researchers, Inc.* (*bacterium*) has widened further. In February two papers, one in *Science*, the other in *Nature*, reported the largest surveys to date of human diversity. Both examined more than 500,000 single nucleotide polymorphisms (SNPs)—swaps of one nucleotide for another at a particular spot in the DNA—from the Human Genome Diversity Panel. These cell lines were drawn from about 1,000 individuals from 51 populations worldwide and are maintained by the Center for the Study of Human Polymorphisms in Paris.

The two research teams analyzed the wealth of data in various ways. They compared SNPs directly among distinct populations. They also looked at haplotypes, blocks of DNA containing numerous SNPs that are inherited intact through many generations. The group that wrote the *Nature* paper also explored a new technique for surveying human variation by comparing repetitions or deletions of DNA stretches of up to 1,000,000 nucleotides long (copy number variations) throughout a person's genome, consistent with the larger trend to mine the genome for ever more markers of variation. "Any one piece of the genome will have a history that doesn't necessarily reflect the ancestry of the genome as a whole," says Noah A. Rosenberg of the University of Michigan at Ann Arbor and lead author of the *Nature* paper. But looking at many areas at once, he explains, can overcome that problem: "With thousands of markers, it's possible to determine the overall story of human migrations."

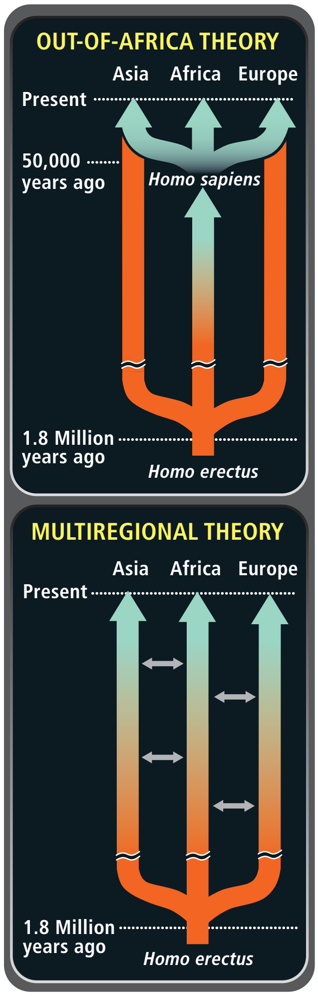
Looking at hundreds of thousands of SNPs allowed the researchers to resolve the identities of individual populations—and to see how genetically close relations spread far and wide. Native South American ancestry was tracked back to Siberians and some other Asians. The Han people, China's principle ethnic group, has distinct northern and southern populations. Bedouins are related to groups from Europe and Pakistan as well as the Middle East.

The findings, which jibed with previous research from anthropology, archaeology, linguistics and biology (including previous mitochondrial and Y DNA studies), also provided a broader statistical foundation for the out-of-Africa hypothesis, supporting the idea that a small population of humans moved out of the continent, then grew in size in a new home until another subgroup of "founders" broke off and moved away—a process that repeated itself until the entire world was settled. These wayfarers edged out archaic human populations—*Homo neanderthalensis* and *Homo erectus*—with little or no interbreeding when they met. The new DNA work indicates that each time a smaller group split off, it carried only a subset of the genetic diversity originally present in the African population. So as distance (and time) removed from Africa lengthens, diversity diminishes, providing a means to follow population movements. Native Americans, sojourners on the last major continental migrations, have much less variety in their genomes than Africans do.

Many scientists believe that the weight of evidence, now backed by large statistical analyses such as the ones in *Science* and *Nature*, gives the out-of-Africa proponents a clear edge in a long-running debate over human origins. The multiregional hypothesis—a competitor to the out-of-Africa one—argues that populations that descended from archaics, such as *H. erectus*, evolved over the past 1.8 million years in Africa, Europe and Asia, and gradually emerged as *Homo sapiens*. Occasional interbreeding ensured that the groups did not split off into separate species.

Few scientists still hold a banner for a strict interpretation of multiregionalism. But modified versions still circulate, mostly as attempts to pinpoint whether *H. sapiens* bear genetic signatures of our encounters with hominid cousins. Vinayak Eswaran of the Indian Institute of Technology, aided by Henry C. Harpending and Alan R. Rogers of the University of Utah, came up with a set of simulations in recent years that suggest that after humans migrated out of Africa they interbred extensively with archaic species such as *H. erectus*. Eswaran's model suggests that as much as 80 percent of the modern human genome may have been subject to the effects of this kind of interbreeding.

The genetic imprint is not as visible as might be expected if interbreeding occurred, but Harpending offers an explanation. A set of beneficial genes carried by African emigrants, perhaps ones that assisted in childbearing, brought a selective advantage that eventually blotted out the signature of some archaic genes. "The result is that the population seems more closely related to the [African] source population of the favored genes than it really is," he says.



DUELING THEORIES

The out-of-Africa theory postulates that humans with modern traits left Africa from 50,000 to 60,000 years ago to settle the world. Along the way, they replaced archaic hominids, such as *Homo erectus*, that left Africa as early as 1.8 million years ago. The competing multiregional theory holds that modern characteristics evolved not just in Africa but in archaic hominid populations in Asia and Europe. Interbreeding among all these groups (*horizontal arrows*) ensured that they remained a single species.

JEN CHRISTIANSEN

Are We Part Neandertal?

Eswaran and Harpending are not the only ones suggesting the possibility of interspecies trysts. Some fossilized skeletal remains of *H. sapiens* have features reminiscent of earlier hominids, and the genetic record of contemporary humans has also provided fuel for discussion.

According to the tree diagrams that document genetic lineages, some gene variants show "deep ancestry"—they are much older than they should be if humans evolved from a single homogeneous group no more than 200,000 years ago; a hint of possible interbreeding. In one study that drew attention in 2006, Bruce T. Lahn of the University of Chicago and his colleagues reported that a version of the *Microcephalin* gene, which is involved in regulating brain size, contains a haplotype that may have been passed on during an encounter with Neandertals 40,000 years ago.

A more definitive answer may arrive within the next 12 months. The Neandertal Genome Project—a collaboration of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and 454 Life Sciences, a Connecticut-based sequencing company—is scheduled by the end of this year to have finished a rough draft of some 70 percent of the sequences of DNA from 40,000-year-old Neandertal bones from a Croatian cave. Its results are expected to be published about six months later.

So far the project has unearthed no sign of any genetic pattern that would suggest DNA transfer between the two hominid lineages. "We see no evidence of that, but we can't exclude it," says Svante Pääbo, the Max Planck professor who heads the project. An earlier publication by his group that surveyed one million nucleotides, a minuscule fraction of the whole genome, suggested that some gene exchange might have occurred, but the result was later found to have been a false signal because of sample contamination. The researchers have not yet encountered the *Microcephalin* variant cited by Lahn.

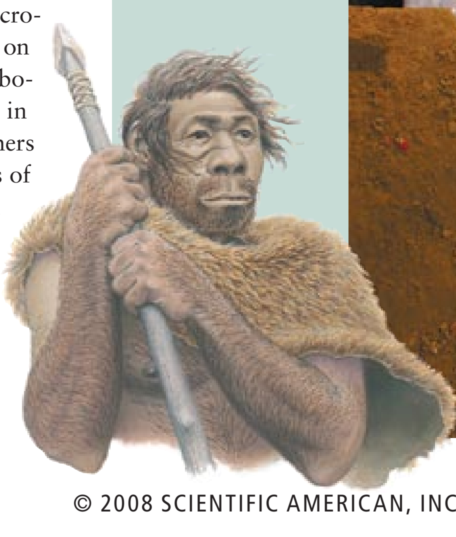
Handling or even breathing on a sample remains an impediment to working with ancient DNA: some anthropologists wrap themselves in the clean-room "bunny suits" used in microchip factories when they head to the field on a dig. Since that initial paper, Pääbo's laboratory has altered the procedures used in the clean room at Max Planck. Researchers place tags made up of four nucleotides of synthetic DNA at the beginning of each strand of Neandertal genetic material. Each strand that exits the sequencing machine goes through a molecular identity check.

An understanding of the genetic makeup of the closest cousin in the human line—estimates from previous studies show that the two genomes are about 99.5 percent alike—could provide the most incisive exercise to date in comparative genomics, allowing identification of sites in the human genome where interbreeding took its course and where natural selection favored certain traits. "I think if you're interested in human evolution, Neandertals are the unique thing," Pääbo says. "They are our closest relatives. You can access their genomes, even though it's technically difficult. But for most other ancestral human groups, that will not be possible."

New, still unpublished work reveals that the Neandertal Y chromosome differs from the human one. "No human man has a Y chromosome like that of the Neandertal," Pääbo observes, mirroring earlier results showing that human and Neandertal mitochondrial DNA also are readily distinguishable. Last November Pääbo and his team did report one similarity between the two hominids. Neandertal remains from Spain had a version of a gene known as

JUST LOOK IN THE PHONE BOOK

The genetic record of human history may be bolstered by simply paging through a phone book for certain names. A team led by Mark A. Jobling of the University of Leicester reported last year that men in northwestern England with surnames that had been used there before 1600 had high levels of Scandinavian ancestry on their Y chromosomes, a legacy of a Viking heritage. Jobling has suggested in another paper that criminal investigators might be able to use this method to link DNA evidence to a set of surnames to narrow down a pool of suspects.



CONTAMINATION from human DNA complicates genetic analyses of Neandertals. Workers in the El Sidron cave in Spain have taken to wearing clean-room suits to protect newly excavated samples.

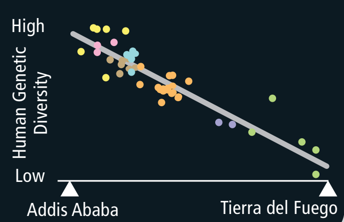
JAY H. MATTERNES (*Neandertal*); EL SIDRON RESEARCH TEAM (*excavation*)

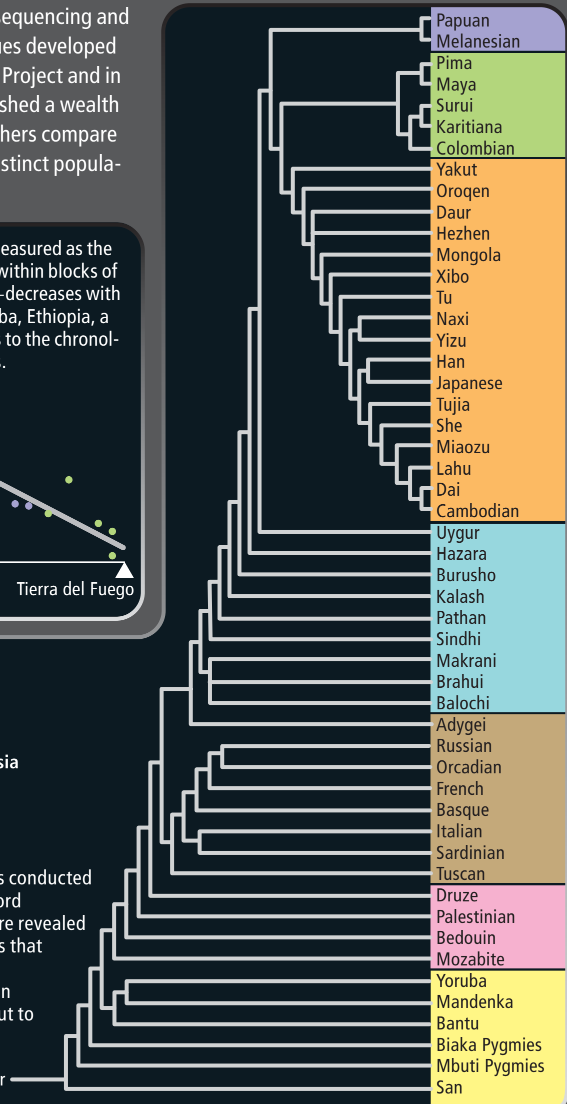
[WHOLE-GENOME RESULTS]

LOOKING FAR AND WIDE

High-powered genetic sequencing and computational techniques developed for the Human Genome Project and in its aftermath have furnished a wealth of data that lets researchers compare genomes drawn from distinct populations around the globe.

The diversity of DNA—measured as the variation of nucleotides within blocks of DNA called haplotypes—decreases with distance from Addis Ababa, Ethiopia, a pattern that corresponds to the chronology of human migrations.





Geographic Region
- Oceania
- Americas
- East Asia
- Central and South Asia
- Europe
- Middle East
- Africa

Whole-genome analysis conducted by researchers at Stanford University and elsewhere revealed many of the populations that form the branches of a genetic tree beginning in Africa and expanding out to the rest of the world.

A genomic map of the world, crafted by researchers at the University of Michigan at Ann Arbor, shows that genetic diversity decreases outside of Africa. Each colored tile represents a common haplotype. Africa has more tiles than found on other continents and ones that correspond to haplotypes found nowhere else.

FOXP2 that is identical to one in humans that is involved with the development of speech and language. Again, speculation emerged in a paper by a separate group in April about whether the gene could have resulted from interbreeding, although the possibility of contamination could not be discounted.

How Have We Adapted?

As researchers continue sequencing DNA from shards of old bone to explore whether humans mated with other species of the genus *Homo*, other investigators are applying genome-wide analyses of DNA to see which genetically controlled traits changed through genetic drift (random mutations) and natural selection as migrants adapted to their new homes.

A study published in February in *Nature* showed the consequences of the declining genetic diversity as humans left Africa. The project compared 40,000 SNPs from a group of 20 European-Americans and 15 African-Americans. It found that the European-Americans had a higher proportion of harmful genetic changes, ones potentially related to disease, than the African-Americans did, although the authors refrained from speculation about any specific health effects. The research shows what lead scientist Carlos D. Bustamante called a "population genetic echo" of Europe's founding. The low genetic diversity of Europe's small initial population permitted a set of harmful mutations to disperse widely and new harmful ones to emerge when the numbers of people began to grow. Natural selection has not yet had time to remove deleterious changes.

Genome-wide research is also starting to furnish a panoramic picture of how natural selection helped migrants adapt to new environs. A spate of studies in the past two years have looked for genetic alterations that have occurred since humans left Africa or took up agriculture and that appear to have been useful for surviving in novel circumstances. Genetic prospectors mined the International HapMap, a catalogue of haplotypes and the 3.9 million SNPs contained therein from North Americans with ancestry in northwestern Europe and from individuals sampled in Nigeria, China and Japan.

One study, co-authored by Harpending, showed that the rate of change of DNA, and thus the pace of evolution, has accelerated over the past 40,000 years. Another by Pardis C. Sabeti of the Broad Institute in Cambridge, Mass., and her colleagues indicated that hundreds of regions

MARTIN SOAVE *University of Michigan at Ann Arbor (map)*; JEN CHRISTIANSEN *(graph and genetic tree)*; SOURCE: *WORLDWIDE HUMAN RELATIONSHIPS INFERRED FROM GENOME-WIDE PATTERNS OF VARIATION*, BY JUN Z. LI ET AL., IN *SCIENCE*, VOL. 319; 2008

[FUTURE CHALLENGES]

Can You Spare Some DNA?

In their quest for a more in-depth picture of human origins, geneticists need more samples from indigenous populations the world over. "There's a need for greater resolution in the data," says Marcus W. Feldman of Stanford University and a co-author of a recent whole-genome comparative analysis. "If you were to give me $1 million tomorrow, I'd find 100 more populations out of the 5,000 we need."

An equal hurdle may be overcoming objections to this kind of research. In 1991 Luigi Luca Cavalli-Sforza and his colleagues outlined a vision for the Human Genome Diversity Project, which would have created a store of cells from 25 unrelated individuals from each of some 400 populations worldwide. The project foundered, however, because of resistance from indigenous groups to providing samples: one group called it a "Vampire Project." Despite extensive informed consent procedures, some groups worried about whether the samples would be used in research for patenting and developing new drugs, which they considered to be a form of biopiracy.

The project never received more than planning support from the federal government, but a more modest version began in this decade, based on cell lines that various population geneticists had brought together on their own from more than 1,000 individuals. This collection, known as the Human Genome Diversity Panel, is stored at the Center for the Study of Human Polymorphisms in Paris. So far it has provided a database containing information on 51 populations that has been used for various studies, including two large, transgenomic investigations reported in *Nature* and *Science* this past February.

Like the Human Genome Diversity Project, the more recent Genographic Project, which intends to gather DNA from 100,000 indigenous people, is also facing opposition. The project has careful protocols for ensuring informed consent in sample gathering, and it does not intend to make collections for medical research. Yet it has still run into resistance, in particular, from Native American groups.

No matter what assurances are given, some groups will be reluctant to yield a cheek swab or blood sample. Investigators in this field may never achieve their goal of obtaining a set of samples that fully reflects every subtle gradation of human genetic diversity. *—G.S.*

COLLECTION OF DNA for the Genographic Project moves forward in Chad. Spencer Wells, who heads the project, takes a cheek swab.

DAVID EVANS *National Geographic*

of the genome are still undergoing selection, including areas that govern resistance to disease and the development of skin color, and hair follicles, which regulate sweat. Such findings imply that human populations are continuing to adapt to regional differences in sun exposure, foods and pathogens they encountered when they left their ancestral African home. And Africans have also evolved as their environs changed.

One of the most recent studies, led by Lluis Quintana-Murci of the Pasteur Institute in Paris, showed that 580 genes, including ones that play a role in diabetes, obesity and hypertension, are undergoing selection differently among the HapMap populations, perhaps explaining geographical differences in disease patterns and providing clues to new targets for developing drugs.

Consideration of the processes underlying human diversity sometimes moves beyond the dimensions of hair follicles and the ability to digest milk. Debate over what constitutes race and ethnicity can quickly enter the picture. What does it mean if a gene variant related to cognition is found more in Europeans than in Africans? Better public understanding of genetics—that a single gene does not act like a light switch that toggles between intelligence and doltishness—may quell misguided speculations.

Genetic literacy will let a term like "Asian" or "Chinese" be replaced by more subtle classifications based on the differences in ancestral genetic makeup found in recent genome-wide scans, such as the distinction between China's southern and northern Han groups. "There is no race," Quintana-Murci says. "What we see [from the standpoint of genetics] is geographical gradients. There are no sharp differences between Europeans and Asians. From Ireland to Japan, there is no sharp boundary where something has changed completely."

The journey through evolutionary history set in place by comparative genomics is still starting. In the meantime, the hunger for more data and more powerful computers and algorithms knows no limits. Amassing larger databases—an international consortium announced in January its intention to sequence 1,000 genomes from various regional populations—will let researchers run ever more realistic simulations of alternative models of human evolution and weigh the probabilities of each one, yielding the best picture yet of who we are and where we came from. ■

➡ MORE TO EXPLORE

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New Developments in the Genetic Evidence for Modern Human Origins. Timothy D. Weaver and Charles C. Roseman in *Evolutionary Anthropology,* Vol. 17, pages 69–80; February 22, 2008.

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Multi-touch screens could improve collaboration without a mouse or keyboard

Hands-on COMPUTING

By Stuart F. Brown

When Apple's iPhone hit the streets last year, it introduced so-called multi-touch screens to the general public. Images on the screen can be moved around with a fingertip and made bigger or smaller by placing two fingertips on the image's edges and then either spreading those fingers apart or bringing them closer together. The tactile pleasure the interface provides beyond its utility quickly brought it accolades. The operations felt intuitive, even sensuous. But in laboratories around the world at the time of the iPhone's launch, multi-touch screens had vastly outgrown two-finger commands. Engineers have developed much larger screens that respond to 10 fingers at once, even to multiple hands from multiple people.

It is easy to imagine how photographers, graphic designers or architects—professionals who must manipulate lots of visual material and who often work in teams—would welcome this multi-touch computing. Yet the technology is already being applied in more far-flung situations in which anyone without any training can reach out during a brainstorming session and move or mark up objects and plans.

Perceptive Pixels

Jeff Han, a consulting computer scientist at New York University and founder of Perceptive Pixel in New York City, is at the forefront of multi-touch technology. Walking into his company's lobby, one is greeted by a three-by-eight-foot flat screen. Han steps up to the electronic wall and unleashes a world of images using nothing but the touch of his fingers. As many as 10 or more video feeds can run simultaneously, and there is no toolbar in sight. When Han wants the display to access different files he taps it twice, bringing up charts or menus that can also be tapped.

Several early adopters have purchased complete systems, including intelligence agencies that need to quickly compare geographically coordinated surveillance images in their war rooms. News anchors on CNN used a big Perceptive Pixel system during coverage of the presidential primaries that boldly displayed all 50 U.S. states; to depict voting results, the anchors, standing in front of the screen, dramatically zoomed in and out of states, even counties, simply by moving their fingers across the map. Looking ahead, Han expects the technology to find a home in graphically intense businesses such as energy trading and medical imaging.

Rudimentary work on multi-touch interfaces dates to the early 1980s, according to Bill Buxton, a principal researcher at Microsoft Research. But around 2000, at N.Y.U., Han began a journey to overcome one of the technology's toughest hurdles: achieving fine-resolution fingertip sensing. The solution required both hardware and software innovations.

Perhaps most fundamental was exploiting an optical effect known as frustrated total internal reflection (FTIR), which is also used in fingerprint-recognition equipment. Han, who describes himself as "a very tactile person," became aware of the effect one day when he was looking through a full glass of water. He noticed how crisply his fingerprint on the outside of the glass appeared when viewed through the water at a

KEY CONCEPTS

- Rather than responding to the presence of a single finger, multi-touch computer screens can follow the instructions of many fingers simultaneously.
- A wall-size screen developed by Perceptive Pixel can respond to as many as 10 fingers or multiple hands. Microsoft and Mitsubishi are offering smaller, specialized systems for hotels, stores, and engineering and design firms.
- Multi-touch computing could one day free us from the mouse as our primary computer interface, the way the mouse freed us from keyboards.

—The Editors

JEFF HAN demonstrates his multi-touch screen, which can respond to the movements of multiple fingers or hands; here he enlarges an image.

BRIAN MARANAN PINEDA (*Han at screen*); APPLE/EPA/CORBIS (*iPhone*)

steep angle. He imagined that an electronic system could optically track fingertips placed on the face of a clear computer monitor. Thus began his six-year absorption with multi-touch interfaces.

He first considered building a very high resolution version of the single-touch screens used in automated teller machines and kiosks, which typically sense the electrical capacitance of a finger touching predefined points on the screen. But tracking a randomly moving finger would have required an insane amount of wiring behind the screen, which also would have limited the screen's functionality. Han ultimately devised a rectangular sheet of clear acrylic that acts like a waveguide, essentially a pipe for light waves. Light-emitting diodes (LEDs) around the edges pump infrared light into the sheet. The light streams through, reflecting internally off the sheet walls, much as light flows though an optical fiber. No light leaks out. But when someone places a finger on one face of the sheet, some of the internally reflecting light beams hit it and scatter off, bouncing through the sheet and out the opposite face. Cameras behind the screen sense this leaking light, or FTIR, revealing the location being touched. The cameras can track this leakage from many points at once.

Han soon discovered that the acrylic panel could also serve as a diffusion screen; a projector behind the panel, linked to a computer, could beam images toward it, and they would diffuse through to the other side. The screen could therefore serve as both an output of imagery and an input of touches made on that imagery.

Sensing the exact location of fingers was one challenge. Devising software routines that could track the finger movements and convert them to instructions for what should be happening with images on the screen was tougher. The half a dozen software developers working with Han had to first write software that would function as a high-performance graphics engine, in part to give the display low latency, or ghosting, when fingers dragged objects quickly across the screen. Then they had to deal with the screen's unorthodox FTIR light output from fingertips sweeping around in random directions.

Deep in the architecture of a computer's operating system is an assumption that a user's inputs will come either from a keyboard or a mouse. Keystrokes are unambiguous; a "q" means "q." The movement of a mouse is expressed as Cartesian coordinates—*x* and *y* locations on a two-dimensional grid. Such methods for representing inputs belong to a general discipline known as the graphical user interface, or GUI. Han's

APPLE'S iPhone introduced multi-touch computing to the masses, but far more capable systems are emerging from laboratories.

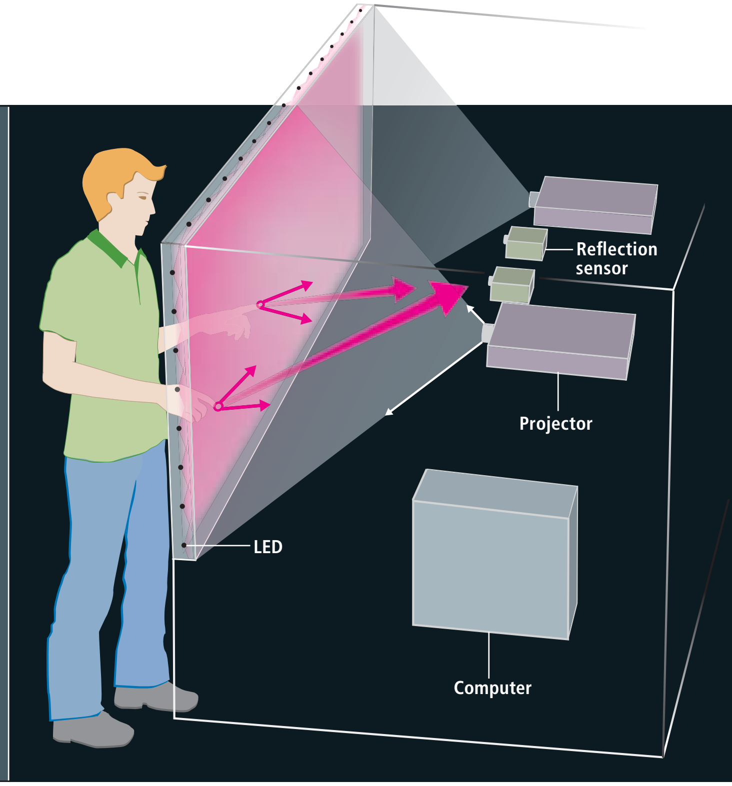
[THE AUTHOR]

Stuart F. Brown is a technology and engineering writer in Irvington, N.Y. He wrote about three-dimensional displays in the *Scientific American* June 2007 issue.

[HOW IT WORKS]

Tracking Fingers

The most advanced multi-touch screens respond to the motion and pressure of numerous fingers. In the Perceptive Pixel design (*near right*), projectors send images through an acrylic screen onto the surface facing the viewer. When fingers or other objects (such as a stylus) touch the surface, infrared light shone inside the acrylic sheet by LEDs scatters off the fingers and back to sensors. Software interprets the data as finger movements. Tapping the screen brings up command menus when desired.



multi-touch screen generates 10 or more streams of *x* and *y* coordinates at the same time, and "the traditional GUIs are really not designed for that much simultaneity," he notes. The current operating systems—Windows, Macintosh, Linux—are so predicated on the single mouse cursor that "we had to tear up a lot of plumbing to make a new multi-touch graphical framework," Han says.

During all this work, Han found that pressure sensing could be accomplished, too, by applying to the front of the acrylic screen a thin layer of polymer with microscopic ridges engineered into its surface. When a user presses harder or more softly on any spot on the polymer, it flexes slightly, and the fingerprint area becomes larger or smaller, causing the scattered light to become brighter or darker, which the camera can sense. By maintaining firm pressure on an object on the screen, a user can slide it behind an adjacent object.

Han's Perceptive Pixel team, formed in 2006, put all the elements together and demonstrated the system at the TED (for *t*echnology, *e*ntertainment and *d*esign) conference that year to an enthusiastic audience. Since then, orders for the system have steadily increased. Perceptive Pixel is not disclosing prices.

Microsoft Scratches the Surface

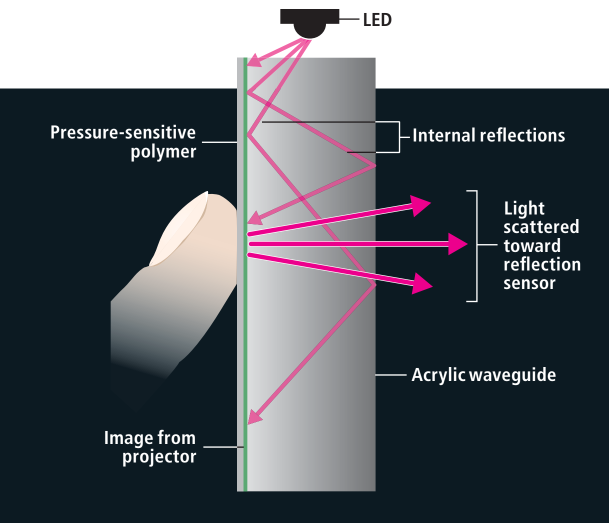
While Han was perfecting his setup, engineers elsewhere were pursuing similar goals by different means. Software giant Microsoft is now rolling out a smaller multi-touch computer called Surface and is trying to brand this category of hardware as "surface computers." The initiative dates back to 2001, when Stevie Bathiche of Microsoft Hardware and Andy Wilson of Microsoft Research began developing an interactive tabletop that could recognize certain physical objects placed on it. The two innovators envisioned that the tabletop could function as an electronic pinball machine, a video puzzle or a photo browser.

More than 85 prototypes later, the pair ended up with a table that has a clear acrylic top and houses a projector on the floor below [*see bottom box on opposite page*]. The projector sends imagery up onto the horizontal, 30-inch screen. An infrared LED shines light up to the tabletop as well, which bounces off fingertips or objects on the other side, thus allowing the device to recognize commands from people's fingers. A Windows Vista computer provides the processing.

Microsoft is shipping Surface table computers to four partners in the leisure, retail and entertainment industries, which it believes are most likely to apply the technology. Starwood Hotels' Sheraton chain, for example, will try installing surface computers in hotel lobbies that will let guests browse and listen to music, send home digital photographs, or order food and drinks. Customers in T-Mobile USA's retail stores will be able to compare different cell phone models by simply placing them atop a surface screen; black-dotted "domino" tags on the undersides of the

CNN ANCHOR **John King uses a Perceptive Pixel screen to explain detailed results of the Texas Democratic primary.**

NILES A. JAEGER (*Brown*); PERCEPTIVE PIXEL (*bottom*); ILLUSTRATIONS BY MELISSA THOMAS



To create a signal, LEDs bounce light through the acrylic sheet. No light escapes. But if a finger is placed against the face (*above*), light will scatter off it toward the sensors. Also, a pressure-sensitive coating flexes when pressed firmly or lightly, making the scattered fingertip signal appear slightly brighter or dimmer, which the computer interprets as more or less pressure.

phones will cue the system to display price, feature and phone plan details. Other Microsoft software will allow a wireless-enabled digital camera, when placed on a surface computer, to upload its photographic content to the computer without a cable.

First-generation surface systems are priced from $5,000 to $10,000. As with most electronic items, the company expects the price to decline as production volume increases. Microsoft says Surface computers should be available at consumer prices in three to five years.

Mitsubishi Wired In, Too

Technology developers might be interested in the DiamondTouch table from a start-up company called Circle Twelve in Framingham, Mass., that was recently spun off from Mitsubishi Electric Research Laboratories. The table, developed at Mitsubishi, is configured so that outside parties can write software for applications they envision; several dozen tables are already in the hands of academic researchers and commercial customers.

The purpose of DiamondTouch "is to support small-group collaboration," says Adam Bogue, Mitsubishi's vice president of marketing. "Multiple people can interact, and the system knows who's who." Several people sit in chairs that are positioned around the table and are linked to a computer below. When one of them touches the tabletop, an array of antennas embedded in the screen sends an extremely small amount of radio-frequency energy through the person's body and chair to a receiver in the computer, a scheme known as capacitive coupling. Alternatively, a special floor mat can be used to complete the circuit. The antennas that are coupled indicate the spot on the screen that the person is touching.

Though seemingly restrictive, this setup can keep track of who makes what inputs, and it can give control to whoever touches the screen first. In that case it will ignore other touches, sensed through the assigned seating, until the first user has completed his or her inputs. The system can also track who makes which annotations to images, such as blueprints.

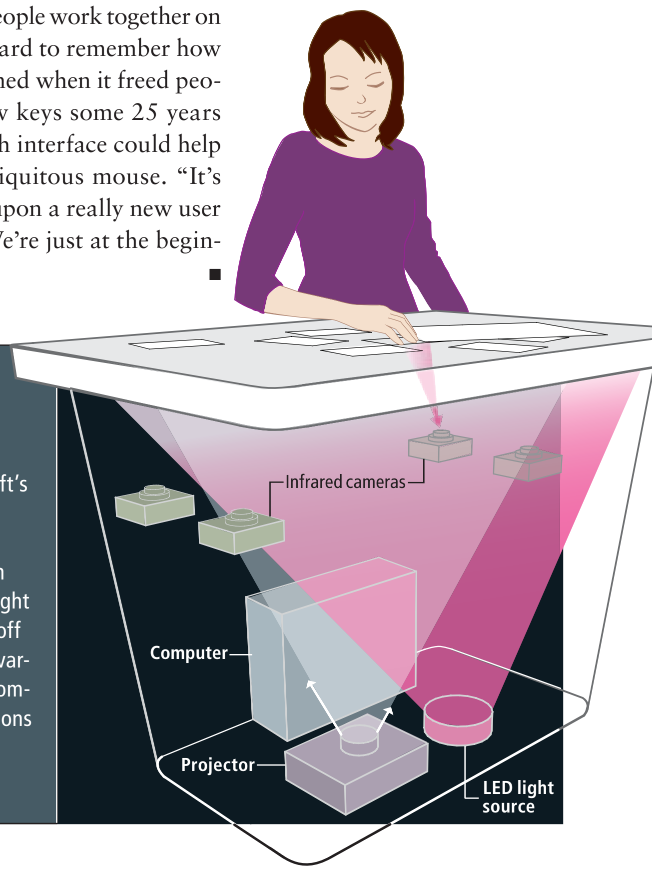
Parsons Brinckerhoff, a global engineering firm headquartered in New York City, has been experimenting with the tables and plans to acquire more. "We have thousands of meetings during the course of a big project," says Timothy Case, the company's visualization department regional manager. "We could have multiple tables in multiple locations, and everybody can be looking at the same thing."

Both the DiamondTouch and Perceptive Pixel systems feature keyboard "emulators" that shine a virtual keyboard onto the screen so that people can type. But it seems unlikely that enthusiasts would prefer to use the dynamic systems for this mundane activity. The great strength of multi-touch is letting multiple people work together on a complex activity. It is hard to remember how liberating the mouse seemed when it freed people from keyboard arrow keys some 25 years ago. Soon the multi-touch interface could help untether us from the ubiquitous mouse. "It's very rare that you come upon a really new user interface," Han says. "We're just at the beginning of this whole thing." ■

[INSIDE LOOK]

Touch Table

A projector inside Microsoft's multi-touch table, called Surface, sends imagery up through the acrylic top. An LED shines near-infrared light up as well, which reflects off objects or fingers back to various infrared cameras; a computer monitors the reflections to track finger motions.



MORE TO EXPLORE

Find a detailed history of multi-touch systems at **www.billbuxton.com/multitouchOverview.html**

View a video demonstration of the Perceptive Pixel system at **www.perceptivepixel.com**

No-Till: the Quiet Revolution

The age-old practice of turning the soil before planting a new crop is a leading cause of farmland degradation. Many farmers are thus looking to make plowing a thing of the past

By David R. Huggins and John P. Reganold

NO-TILL PIONEER John Aeschliman began experimenting with the technique in 1974 out of concern over the soil erosion that was taking place in Washington State's sloping Palouse region, where his farm is located.

ANDY ANDERSON

John Aeschliman turns over a shovelful of topsoil on his 4,000-acre farm in the Palouse region of eastern Washington State. The black earth crumbles easily, revealing a porous structure and an abundance of organic matter that facilitate root growth. Loads of earthworms are visible, too—another healthy sign.

Thirty-four years ago only a few earthworms, if any, could be found in a spadeful of his soil. Back then, Aeschliman would plow the fields before each planting, burying the residues from the previous crop and readying the ground for the next one. The hilly Palouse region had been farmed that way for decades. But the tillage was taking a toll on the Palouse, and its famously fertile soil was eroding at an alarming rate. Convinced that there had to be a better way to work the land, Aeschliman decided to experiment in 1974 with an emerging method known as no-till farming.

Most farmers worldwide plow their land in preparation for sowing crops. The practice of turning the soil before planting buries crop residues, animal manure and troublesome weeds and also aerates and warms the soil. But clearing and disturbing the soil in this way can also leave it vulnerable to erosion by wind and water. Tillage is a root cause of agricultural land degradation—one of the most serious environmental problems worldwide—which poses a threat to food production and rural livelihoods, particularly in poor and densely populated areas of the developing world [see "Pay Dirt," by David R. Montgomery, on page 76]. By the late 1970s in the Palouse, soil erosion had removed 100 percent of the topsoil from 10 percent of the cropland, along with another 25 to 75 percent of the topsoil from another 60 percent of that land. Furthermore, tillage can promote the runoff of sediment, fertilizers and pesticides into rivers, lakes and oceans. No-till farming, in contrast, seeks to minimize soil disruption. Practitioners leave crop residue on the fields after harvest, where it acts as a mulch to protect the soil from erosion and fosters soil productivity. To sow the seeds, farmers use specially designed seeders that penetrate through the residue to the undisturbed soil below, where the seeds can germinate and surface as the new crop.

In its efforts to feed a growing world population, agriculture has expanded, resulting in a greater impact on the environment, human health and biodiversity. But given our current knowledge of the planet's capacity, we now realize that producing enough food is not enough—

KEY CONCEPTS

- Conventional plow-based farming leaves soil vulnerable to erosion and promotes agricultural runoff.
- Growers in some parts of the world are thus turning to a sustainable approach known as no-till that minimizes soil disturbance.
- High equipment costs and a steep learning curve, among other factors, are hindering widespread adoption of no-till practices.

—The Editors

[HISTORY]

AGRICULTURE MILESTONES

The roots of both no-till and tillage-based farming methods run deep, but eventually the latter approach predominated, thanks to the evolution of the plow. Over the past few decades, however, advances in herbicides and machinery have made no-till practical on a commercial scale.

8000 B.C.

Planting stick, the earliest version of no-till, enables the planting of seeds without cultivation.

Scratch plow
the earliest plow, clears a path through the ground cover and creates a furrow into which seeds can be placed.

6000 B.C.

Draft animals replace humans in powering the plow.

3500 B.C.

Plowshare, a wedge-shaped implement tipped with an iron blade, loosens the top layer of soil.

1100 A.D.?

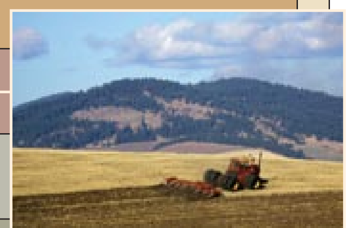
Moldboard plow
has a curved blade (the moldboard) that inverts the soil, burying weeds and residues.

Mid-1800s

Steel moldboard plow
invented by John Deere in 1837, is able to break up prairie sod.

Early 1900s

Tractors
can pull multiple plows at once.



1940s–1950s

Herbicides such as 2,4-D,atrazine and paraquat enable farmers to manage weeds with less tillage.

1960s

No-till seeders
slice open a small groove for seeds, keeping soil disturbance to a minimum.

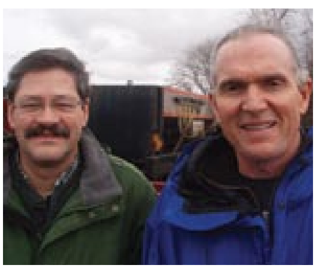
it must also be done sustainably. Farmers need to generate adequate crop yields of high quality, conserve natural resources for future generations, make enough money to live on, and be socially just to their workers and community [see "Sustainable Agriculture," by John P. Reganold, Robert I. Papendick and James F. Parr; Scientific American, June 1990]. No-till farming is one system that has the potential to help realize this vision of a more sustainable agriculture. As with any new system, there are challenges and trade-offs with no-till. Nevertheless, growers in some parts of the world are increasingly abandoning their plows.

Plowing Ahead

People have used both no-till and tillage-based methods to produce food from the earth ever since they started growing their own crops around 10,000 years ago. In the transition from hunting and gathering to raising crops, our Neolithic predecessors planted garden plots near their dwellings and foraged for other foods in the wild. Some performed the earliest version of no-till by punching holes in the land with a stick, dropping seeds in each divot and then covering it with soil. Others scratched the ground with a stick, an incipient form of tillage, to place seeds under the surface. Thousands of farmers in developing countries still use these simple methods to sow their crops.

In time, working the soil mechanically became the standard for planting crops and controlling weeds, thanks to the advent of the plow, which permitted the labor of a few to sustain many. The first such tools were scratch plows, consisting of a frame holding a vertical wooden post that was dragged through the top-

[THE AUTHORS]



David R. Huggins (*left*) is a soil scientist with the USDA-Agricultural Research Service, Land Management and Water Conservation Research Unit in Pullman, Wash. He specializes in conservation cropping systems and their influence on the cycling and flow of soil carbon and nitrogen. John P. Reganold (*right*), Regents Professor of Soil Science at Washington State University at Pullman, specializes in sustainable agriculture. This is his third article for *Scientific American.*

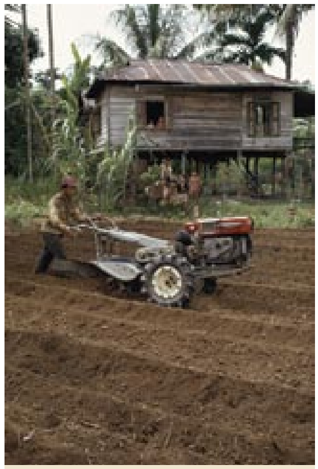
STEWART HIGGINS *Washington State University (Huggins and Reganold)*; WU HONG *EPA/Corbis (scratch plow)*; RALF ROLETSCHEK *(moldboard plow)*; HUGH TALMAN *Smithsonian Images (John Deere plow)*; LANE LAMBERT *iStockPhoto (tractor)*; ANDY ANDERSON *(no-till seeder)*

soil. Two people probably operated the earliest version of this device, one pulling the tool and the other guiding it. But the domestication of draft animals—such as oxen in Mesopotamia, perhaps as early as 6000 B.C.—replaced human power. The next major development occurred around 3500 B.C., when the Egyptians and the Sumerians created the plowshare—a wedge-shaped wooden implement tipped with an iron blade that could loosen the top layer of soil. By the 11th century, the Europeans were using an elaboration of this innovation that included a curved blade called a moldboard that turned the soil over once it was broken open.

Continuing advancements in plow design enabled the explosion of pioneer agriculture during the mid-1800s; farmers cultivated grass-dominated native prairies in eastern Europe, South Africa, Canada, Australia, New Zealand and the U.S., converting them to corn, wheat and other crops. One such region, the tall-grass prairie of the Midwestern U.S., had resisted widespread farming because its thick, sticky sod was a barrier to cultivation. But in 1837 an Illinois blacksmith named John Deere invented a smooth, steel moldboard plow that could break up the sod. Today this former grassland, which includes much of the famous Corn Belt, is home to one of the most agriculturally productive areas in the world.

Agricultural mechanization continued through the early 1900s with the development of many tools that helped farmers cultivate the earth ever more intensively, including tractors that could pull multiple plows at once. Tillage practices were about to undergo profound scrutiny, however. The Dust Bowl era between 1931 and 1939 exposed the vulnerability of plow-based agriculture, as wind blew away precious topsoil from the drought-ravaged southern plains of the U.S., leaving behind failed crops and farms. Thus, the soil conservation movement was born, and agriculturalists began to explore reduced tillage methods that preserve crop residues as a protective ground cover. Spurring the movement was the controversial publication in 1943 of *Plowman's Folly,* by agronomist Edward Faulkner, who challenged the necessity of the plow. Faulkner's radical proposition became more tenable with the development of herbicides—such as 2,4-D, atrazine and paraquat—after World War II, and research on modern methods of no-till agriculture began in earnest during the 1960s.

Considering the pivotal role the plow has come to play in farming, conceiving a way to do without it has proved quite challenging, requiring the reinvention of virtually every aspect of agricultural production. But specially designed seeders have been evolving since the 1960s to meet the unique mechanization requirements of no-till farming. These new seeders, along with chemical herbicides, are two of the main technologies that have at last enabled growers to effectively practice no-till on a commercial scale.



DEAN CONGER *National Geographic/Getty Images*

ADOPTION HURDLES

Although no-till is theoretically applicable to most farmland around the world, the cost of the requisite equipment and herbicides is prohibitive for many growers, most of whom have small farms. Necessary costs aside, poverty itself leads these farmers to use crop residues and animal dung for fuel, for example, and to till the land for short-term gains rather than investing in long-term stewardship.

Of 525 million farms worldwide, roughly 85 percent are less than five acres. The overwhelming majority of these small farms—about 87 percent—are located in Asia (*above*); Africa is home to 8 percent. The adoption of no-till farming in these regions, where the potential benefits are the greatest, is practically negligible.

Signing Up for No-Till

Farmers today prepare for planting in ways that disturb the soil to varying degrees. Tillage with a moldboard plow completely turns over the first six to 10 inches of soil, burying most of the residue. A chisel plow, meanwhile, only fractures the topsoil and preserves more surface residue. In contrast, no-till methods merely create in each planted row a groove just half an inch to three inches across into which seeds can be dropped, resulting in minimal overall soil disturbance. In the U.S., no-till agriculture fits under the broader U.S. Department of Agriculture definition of conservation tillage. Conservation tillage includes any method that retains enough of the previous crop residues such that at least 30 percent of the soil surface is covered after planting. The protective effects of such residues are considerable. According to the USDA's National Resources Inventory data, soil erosion from water and wind on U.S. cropland decreased 43 percent between 1982 and 2003, with much of this decline coming from the adoption of conservation tillage.

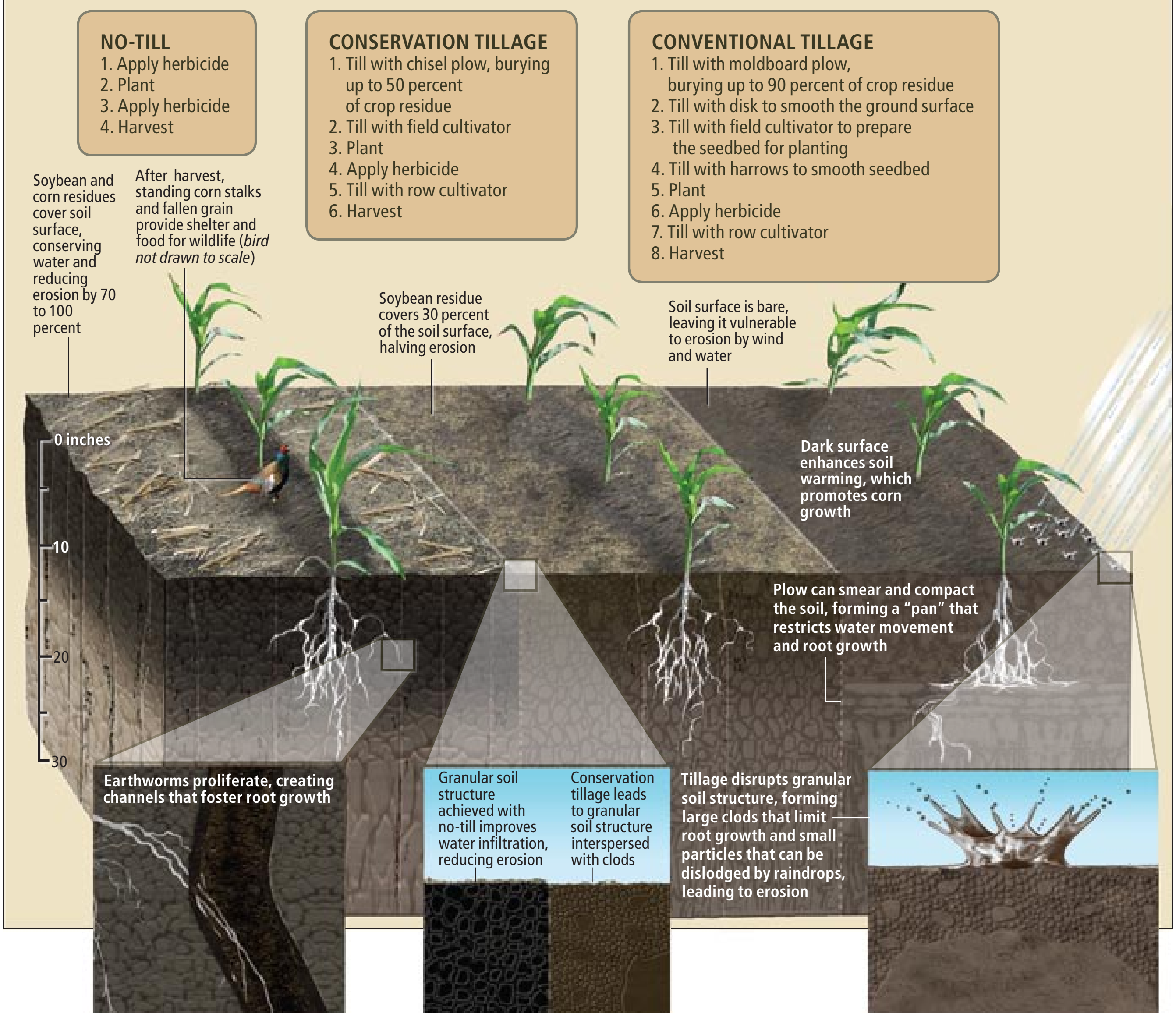
Soil protection is not the only benefit of no-till. Leaving crop residues on the soil surface helps to increase water infiltration and limit runoff. Decreased runoff, in turn, can reduce pollution of nearby water sources with transported sediment, fertilizers and pesticides. The residues also promote water conservation by reducing evaporation. In instances where water availability limits crop production, greater water conservation can mean higher-yielding crops or new capabilities to grow alternative crops.

The no-till approach also fosters the diversity of soil flora and fauna by providing soil organisms, such as earthworms, with food from the residues and by stabilizing their habitat. Together with associated increases in soil organic matter, these conditions encourage soils to develop a more stable internal structure, further improving the overall capacity to grow crops and to buffer them against stresses caused by farming

[A PRIMER]

HOW NO-TILL STACKS UP

Three farming systems for a corn-soybean crop rotation in the U.S. Corn Belt are contrasted here. No-till requires the fewest passes over a field.



operations or environmental hazards. No-till can thus enable the more sustainable farming of moderately to steeply sloping lands that are at elevated risk of erosion and other problems.

Wildlife, too, gains from no-till, because standing crop residues and inevitable harvest losses of grain provide cover and food for upland game birds and other species. In a study published in 1986, researchers in Iowa found 12 bird species nesting in no-till fields, compared with three species in tilled fields.

Furthermore, reducing tillage increases soil carbon sequestration, compared with conventional moldboard plowing. One of agriculture's main greenhouse gas mitigation strategies is soil carbon sequestration, wherein crops remove carbon dioxide from the atmosphere during photosynthesis, and nonharvested residues and roots are converted to soil organic matter, which is 58 percent carbon. About half of the overall potential for U.S. croplands to sequester soil carbon comes from conservation tillage, including no-till.

In addition, no-till can offer economic advantages to farmers. The number of passes over a field needed to establish and harvest a crop with no-till typically decreases from seven or more to four or fewer. As such, it requires 50 to 80 per-

KEVIN HAND

cent less fuel and 30 to 50 percent less labor than tillage-based agriculture, significantly lowering production costs per acre. Although specialized no-till seeding equipment can be expensive, with some sophisticated seeders priced at more than $100,000, running and maintaining other tillage equipment is no longer necessary, lowering the total capital and operating costs of machinery required for crop establishment by up to 50 percent. With these savings in time and money, farmers can be more competitive at smaller scales, or they can expand and farm more acres, sometimes doubling farm size using the same equipment and labor. Furthermore, many farmers appreciate that the time they once devoted to rather mundane tillage tasks they can instead spend on more challenging aspects of farming, family life or recreation, thereby enhancing their overall quality of life.

Betting the Farm

No-till and other conservation tillage systems can work in a wide range of climates, soils and geographic areas. Continuous no-till is also applicable to most crops, with the notable exceptions of wetland rice and root crops, such as potatoes. Yet in 2004, the most recent year for which data are available, farmers were practicing no-till on only 236 million acres worldwide—not even 7 percent of total global cropland.

Of the top five countries with the largest areas under no-till, the U.S. ranks first, followed by Brazil, Argentina, Canada and Australia. About 85 percent of this no-till land lies in North and South America. In the U.S., roughly 41 percent of all planted cropland was farmed using conservation tillage systems in 2004, compared with 26 percent in 1990. Most of that growth came from expanded adoption of no-till, which more than tripled in that time, to the point where it was practiced on 22 percent of U.S. farmland. This no doubt partly reflects the fact that U.S. farmers are encouraged to meet the definition of conservation tillage to participate in government subsidy and other programs. In South America, adoption of no-till farming has been relatively rapid as a result of coordinated efforts by university agricultural-extension educators and local farm communities to develop viable no-till cropping systems tailored to their particular needs.

On the other hand, adoption rates are low in Europe, Africa and most parts of Asia. Embracing no-till has been especially difficult in developing countries in Africa and Asia, because farmers there often use the crop residues for fuel, animal feed and other purposes. Furthermore, the specialized seeders required for sowing crops and the herbicides needed for weed control may not be available or can be prohibitively expensive for growers in these parts of the world. Meanwhile, in Europe, an absence of government policies promoting no-till, along with elevated restrictions on pesticides (including herbicides), among other variables, leaves farmers with little incentive to adopt this approach.

Changing from tillage-based farming to no-till is not easy. The difficulty of the transition, together with the common perception that no-till incurs a greater risk of crop failure or lower net returns than conventional agriculture, has seriously hindered more widespread adoption of this approach. Although farmers accept that agriculture is not a fail-safe profession, they will hesitate to adopt a new farming practice if the risk of failure is greater than in conventional practice. Because no-till is a radical departure from other farming practices, growers making the switch to no-till experience a steep learning curve. In addition to the demands of different field practices, the conversion has profound impacts on farm soils and fields. Different pest species can arise with the shift from tillage-based agriculture to no-till, for instance. And the kinds of weeds and crop diseases can change. For example, the elevated moisture levels associated with no-till can promote soil-borne fungal diseases that tillage previously kept in check. Indeed, the discovery of new crop diseases has sometimes accompanied the shift to no-till.

Some of the changes that follow from no-till can take years or even decades to unfold, and farmers need to remain vigilant and adaptable to new, sometimes unexpected, situations, such as those that arise from shifts in soil and residue conditions or fertilizer management. During this transition, there is a real risk of reduced yields and even failed crops. In the Palouse, for example, some farmers who attempted no-till in the 1980s are no longer in business. Consequently, farmers looking to switch to no-till should initially limit the converted acreage to 10 to 15 percent of their total farm.

Farmers who are new to no-till techniques often visit successful operations and form local or regional support groups, where they share experiences and discuss specific problems. But the advice they receive in areas with limited no-till adoption can be incomplete or contradictory,

TWO SIDES OF NO-TILL

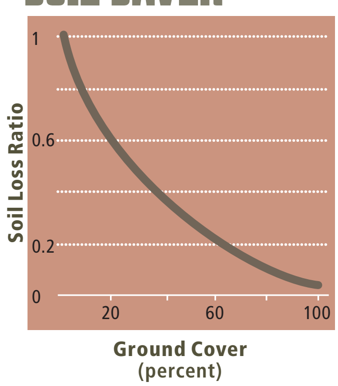
PAYOFFS

- Reduces soil erosion
- Conserves water
- Improves soil health
- Reduces fuel and labor costs
- Reduces sediment and fertilizer pollution of lakes and streams
- Sequesters carbon

TRADE-OFFS

- Transition from conventional farming to no-till is difficult
- Necessary equipment is costly
- Heavier reliance on herbicides
- Prevalence of weeds, disease and other pests may shift in unexpected ways
- May initially require more nitrogen fertilizer
- Can slow germination and reduce yields

SOIL SAVER



LEAVING 30 PERCENT of the soil surface covered with residue reduces erosion by half as compared with bare, fallow soil. And leaving 50 to 100 percent of the surface covered throughout the year, as no-till does, reduces soil erosion dramatically.

DANIELA NAOMI MOLNAR

and gaps in knowledge, experience or technology can have potentially disastrous outcomes. If the perception that no-till is riskier than conventional techniques develops in a farming community, banks may not underwrite a no-till farmer's loan. Alternatively, growers who are leasing land may find that the owners are opposed to no-till because of fears that they will not get paid as much. Improving the quality of information exchange among farmers, universities, agribusinesses and government agencies will no doubt go a long way toward overcoming these obstacles.

Yet even in the hands of a seasoned no-till farmer, the system has drawbacks. No-till crop production on fine-textured, poorly drained soils can be particularly problematic, often resulting in decreased yields. Yields of no-till corn, for instance, are often reduced by 5 to 10

[A CASE FOR NO-TILL]

PAY DIRT

The slow pace at which soil rebuilds makes its conservation essential **By David R. Montgomery**

A fundamental drawback of conventional farming is that it fosters topsoil erosion, especially on sloping land. Tillage leaves the ground surface bare and vulnerable to runoff, and each pass of the plow pushes soil downhill. As a result, the soil thins over time. How long this process takes depends not only on how fast plowing pushes soil downhill—and wind or runoff carries it away—but also on how fast the underlying rocks break down to form new soil.

In the 1950s, when the Soil Conservation Service (now known as the Natural Resources Conservation Service) began defining tolerable rates of soil erosion from agricultural land, hardly any data on rates of soil production were available. The agency thus determined the so-called soil loss tolerance values, or T values, on the basis of what farmers could do to reduce erosion without "undue economic impact" using conventional farming equipment. These T values correspond to as much as an inch of erosion in 25 years. But recent research has shown that erosion rate to be far faster than the rate at which soil rebuilds.

Over the past several decades, scientists have determined that measuring the soil concentrations of certain isotopes that form at a known rate permits direct quantification of soil production rates. Applying this technique to soils in temperate regions in coastal California and southeastern Australia, geologist Arjun Heimsath of Arizona State University and his colleagues found soil production rates ranging from 0.00118 to 0.00315 inch a year. As such, it takes 300 to 850 years to form an inch of soil in these places. My own recent global compilation of data from soil production studies, published last year in the *Proceedings of the National Academy of Sciences USA,* revealed an average rate of 0.00067 to 0.00142 inch a year—equivalent to 700 to 1,500 years to form an inch of soil.

The soil on undisturbed hillsides in temperate and tropical latitudes is generally one to three feet thick. With natural soil production rates of centuries to millennia per inch and soil erosion rates of inches per century under plow-based agriculture, it would take just several hundred to a couple of thousand years to plow through the soil in these regions. This simple estimate predicts remarkably well the life span of major agricultural civilizations around the world. With the exception of the fertile river valleys along which agriculture began, civilizations generally lasted 800 to 2,000 years, and geoarchaeological studies have now shown a connection between soil erosion and the decline of many ancient cultures.

Clearly, then, if we are to conserve resources for future generations, we need alternatives to conventional farming practices. No-till systems simultaneously reduce the erosive force of runoff and increase the ability of the ground to hold onto soil, making these methods remarkably effective at curbing erosion. In a study published in 1993, researchers at the University of Kentucky found that no-till methods decreased soil erosion by a whopping 98 percent. More recently, investigators at the University of Tennessee reported that no-till tobacco farming reduced soil erosion by more than 90 percent over conventional tobacco cultivation. Although the effect of no-till on erosion rates depends on a number of local factors, such as the type of soil and the crop, it can bring soil erosion rates down close to soil production rates.

In the mid-1990s Cornell University researchers estimated that undoing damage caused by soil erosion would cost the U.S. $44 billion a year, and that it would take an annual investment of about $6 billion to bring erosion rates on U.S. cropland in line with soil production. They also estimated that each dollar invested in soil conservation would save society more than $5. Because it is prohibitively expensive to put soil back on the fields once it leaves, the best, most cost-effective strategy for society at large is to keep it on the fields in the first place.

WIND EROSION in the Southern Plains of the U.S. during the Dust Bowl era revealed the perils of plow-based farming.

GETTY IMAGES

David R. Montgomery is a professor of geomorphology at the University of Washington and author of Dirt: The Erosion of Civilizations.

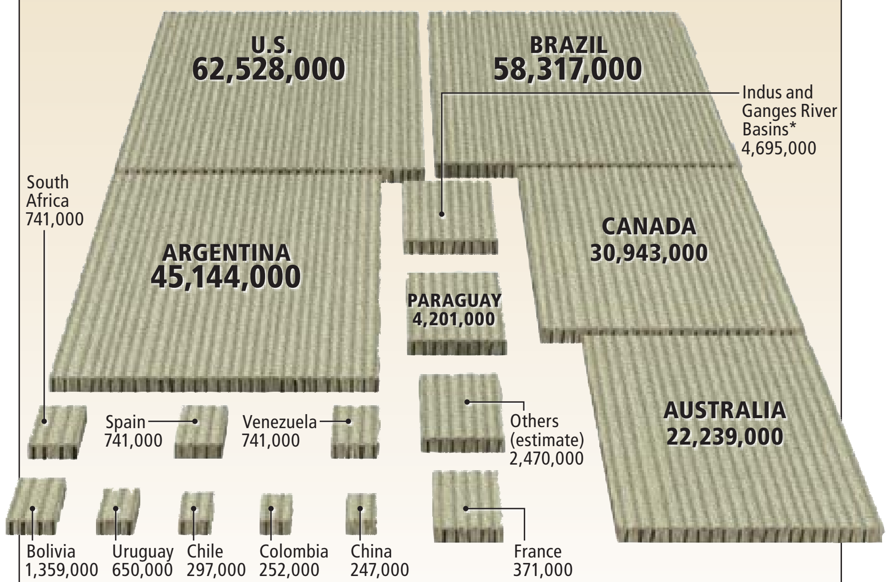
percent on these kinds of soils, compared with yields with conventional tillage, particularly in northern regions. And because the crop residue blocks the sun's rays from warming the earth to the same degree as occurs with conventional tillage, soil temperatures are colder in the spring, which can slow seed germination and curtail the early growth of warm-season crops, such as corn, in northern latitudes.

In the first four to six years, no-till demands the use of extra nitrogen fertilizer to meet the nutritional requirements of some crops, too—up to 20 percent more than is used in conventional tillage systems—because increasing organic matter at the surface immobilizes nutrients, including nitrogen. And in the absence of tillage, farmers depend more heavily on herbicides to keep weeds at bay. Herbicide-resistant weeds are already becoming more common on no-till farms. The continued practice of no-till is therefore highly dependent on the development of new herbicide formulations and other weed management options. Cost aside, greater reliance on agrichemicals may adversely affect nontarget species or contaminate air, water and soil.

[WHERE IT IS USED]

NO-TILL ACREAGE

Less than 7 percent of the world's cropland is farmed using no-till methods. Of these 236 million acres, about 85 percent are in North and South America.



*Encompasses much of India, Pakistan and Bangladesh.

SOURCE: United Nations Food and Agriculture Organization. Data from 2004.

Integrating No-Till

No-till has the potential to deliver a host of benefits that are increasingly desirable in a world facing population growth, environmental degradation, rising energy costs and climate change, among other daunting challenges. But no-till is not a cure-all; such a thing does not exist in agriculture. Rather it is part of a larger, evolving vision of sustainable agriculture, in which a diversity of farming methods from no-till to organic—and combinations thereof—is considered healthy. We think that ultimately all farmers should integrate conservation tillage, and no-till if feasible, on their farms.

Future no-till farming will need to employ more diverse pest and weed management strategies, including biological, physical and chemical measures to lessen the threat of pesticide resistance. Practices from successful organic farming systems may be instructive in that regard. One such technique, crop rotation—in which farmers grow a series of different crops in the same space in sequential seasons—is already helping no-till's war on pests and weeds by helping to break up the weed, pest and disease cycles that arise when one species is continuously grown.

To that end, the capacity to grow a diverse selection of economically viable crops would advance no-till farming and make it more appealing to farmers. But the current emphasis on corn to produce ethanol in the Midwestern Corn Belt, for instance, is promoting monoculture—in which a single crop, such as corn, is grown over a wide area and replanted every year—and will likely make no-till farming more difficult in this region. Experts continue to debate the merits of growing fuel on farmland, but if we decide to proceed with biofuel crops, we will need to consider using no-till with crop rotation to produce them sustainably. Development of alternative crops for bioenergy production on marginal lands, including perennials such as switchgrass, could complement and promote no-till farming, as would perennial grain food crops currently under development [see "Future Farming: A Return to Roots?" by Jerry D. Glover, Cindy M. Cox and John P. Reganold; Scientific American, August 2007].

Today, three decades after first attempting no-till on his Palouse farm, John Aeschliman uses the system on 100 percent of his land. His adoption of no-till has followed a gradual, cautious path that has helped minimize his risk of reduced yields and net returns. Consequently, he is one of many farmers, large and small, who is reaping the rewards of no-till farming and helping agriculture evolve toward sustainability. ■

➡ MORE TO EXPLORE

Corn-Soybean Sequence and Tillage Effects on Soil Carbon Dynamics and Storage. David R. Huggins, Raymond R. Allmaras, Charles E. Clapp, John A. Lamb and Gyles W. Randall in *Soil Science Society of America Journal,* Vol. 71, No. 1, pages 145–154; January/February 2007.

Constraints to Adopting No-Till Farming in Developing Countries. Rattan Lal in *Soil & Tillage Research,* Vol. 94, No. 1, pages 1–3; May 2007.

Dirt: The Erosion of Civilizations. David R. Montgomery. University of California Press, 2007.

No-Tillage Seeding in Conservation Agriculture. Second edition. C. John Baker et al. CABI Publishing, 2007.

More information about conservation agriculture from the United Nations Food and Agriculture Organization is available at **www.fao.org/ag/ca**

KEVIN HAND

THE NEUROSCIENCE OF Dance

Recent brain-imaging studies reveal some of the complex neural choreography behind our ability to dance

By Steven Brown and Lawrence M. Parsons

KEY CONCEPTS

- Dance is a fundamental form of human expression that likely evolved together with music as a way of generating rhythm.
- It requires specialized mental skills. One brain area houses a representation of the body's orientation, helping to direct our movements through space; another serves as a synchronizer of sorts, enabling us to pace our actions to music.
- Unconscious entrainment—the process that causes us to absent-mindedly tap our feet to a beat—reflects our instinct for dance. It occurs when certain subcortical brain regions converse, bypassing higher auditory areas.

—The Editors

So natural is our capacity for rhythm that most of us take it for granted: when we hear music, we tap our feet to the beat or rock and sway, often unaware that we are even moving. But this instinct is, for all intents and purposes, an evolutionary novelty among humans. Nothing comparable occurs in other mammals nor probably elsewhere in the animal kingdom. Our talent for unconscious entrainment lies at the core of dance, a confluence of movement, rhythm and gestural representation. By far the most synchronized group practice, dance demands a type of interpersonal coordination in space and time that is almost nonexistent in other social contexts.

Even though dance is a fundamental form of human expression, neuroscientists have given it relatively little consideration. Recently, however, researchers have conducted the first brain-imaging studies of both amateur and professional dancers. These investigations address such questions as, How do dancers navigate though space? How do they pace their steps? How do people learn complex series of patterned movements? The results offer an intriguing glimpse into the complicated mental coordination required to execute even the most basic dance steps.

I Got Rhythm

Neuroscientists have long studied isolated movements such as ankle rotations or finger tapping. From this work we know the basics of how the brain orchestrates simple actions. To hop on one foot—never mind patting your head at the same time—requires calculations relating to spatial awareness, balance, intention and timing, among other things, in the brain's sensorimotor system. In a simplified version of the story, a region called the posterior parietal cortex (toward the back of the brain) translates visual information into motor commands, sending signals forward to motion-planning areas in the premotor cortex and supplementary motor area. These

instructions then project to the primary motor cortex, which generates neural impulses that travel to the spinal cord and on to the muscles to make them contract [*see box on next page*].

At the same time, sensory organs in the muscles provide feedback to the brain, giving the body's exact orientation in space via nerves that pass through the spinal cord to the cerebral cortex. Subcortical circuits in the cerebellum at the back of the brain and in the basal ganglia at the brain's core also help to update motor commands based on sensory feedback and to refine our actual motions. What has remained unclear is whether these same neural mechanisms scale up to enable maneuvers as graceful as, say, a pirouette.

To explore that question, we conducted the first neuroimaging study of dance movement, in conjunction with our colleague Michael J. Martinez of the University of Texas Health Science Center at San Antonio, using amateur tango dancers as subjects. We scanned the brains of five men and five women using positron-emission tomography, which records changes in cerebral blood flow following changes in brain activity; researchers interpret increased blood flow in a specific region as a sign of greater activity among neurons there. Our subjects lay flat inside the scanner, with their heads immobilized, but they were able to move their legs and glide their feet along an inclined surface [*see box on page 81*]. First, we asked them to execute a box step, derived from the basic *salida* step of the Argentine tango, pacing their movements to the beat of instrumental tango songs, which they heard through headphones. We then scanned our dancers while they flexed their leg muscles in time to the music without actually moving their legs. By subtracting the brain activity elicited by this plain flexing from that recorded while they "danced," we were able to home in on brain areas vital to directing the legs through space and generating specific movement patterns.

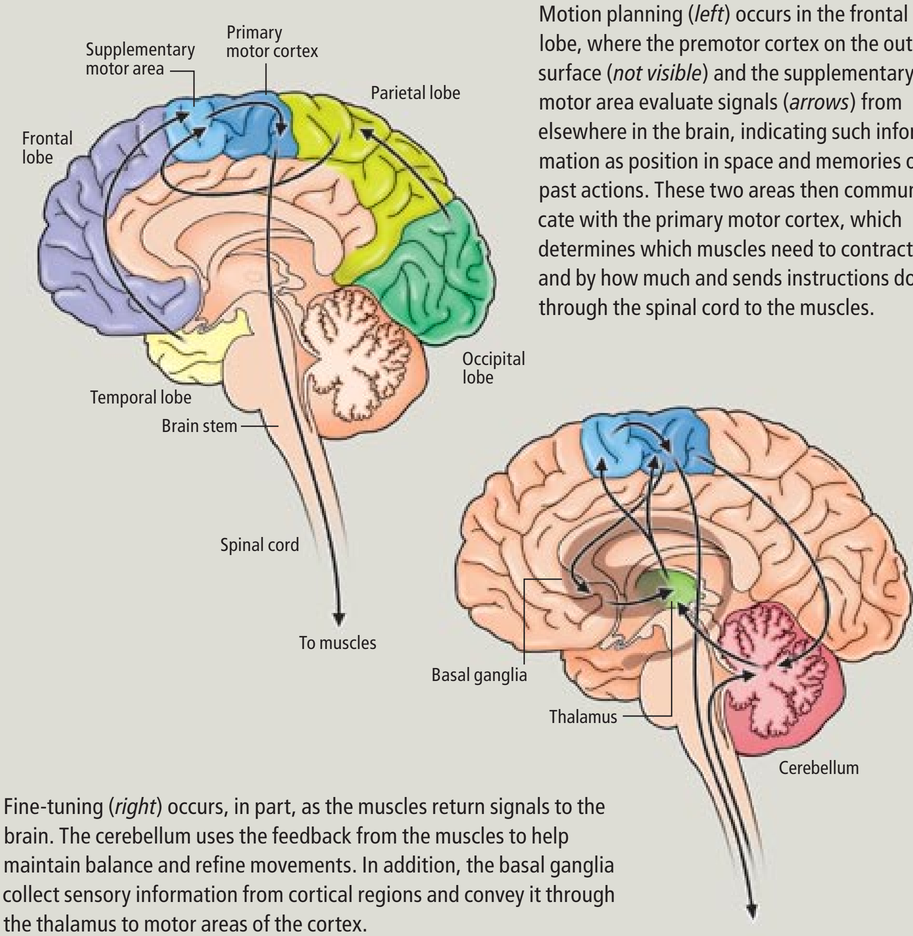
DANCE is the most synchronized activity people perform. Neuroscientists are trying to discover not only how but why we do it.

WOODY WELCH *Aurora Photos*

[THE BASICS]

THE BRAIN'S MOVING PARTS

To identify the brain areas that control dance, researchers first need a sense of how the brain allows us to carry out voluntary movements in general. A highly simplified version is presented here.



Motion planning (*left*) occurs in the frontal lobe, where the premotor cortex on the outer surface (*not visible*) and the supplementary motor area evaluate signals (*arrows*) from elsewhere in the brain, indicating such information as position in space and memories of past actions. These two areas then communicate with the primary motor cortex, which determines which muscles need to contract and by how much and sends instructions down through the spinal cord to the muscles.

Fine-tuning (*right*) occurs, in part, as the muscles return signals to the brain. The cerebellum uses the feedback from the muscles to help maintain balance and refine movements. In addition, the basal ganglia collect sensory information from cortical regions and convey it through the thalamus to motor areas of the cortex.

TANTALIZING TANGO FINDING

In a study published in December 2007, Gammon M. Earhart and Madeleine E. Hackney of the Washington University School of Medicine in St. Louis found that tango dancing improved mobility in patients with Parkinson's disease. The condition stems from a loss of neurons in the basal ganglia, a problem that interrupts messages meant for the motor cortex. As a result, patients experience tremors, rigidity and difficulty initiating movements they have planned.

The researchers found that after 20 tango classes, study subjects "froze" less often. Compared with subjects who attended an exercise class instead, the tango dancers also had better balance and higher scores on the Get Up and Go test, which identifies those at risk for falling.

As anticipated, this comparison eliminated many of the basic motor areas of the brain. What remained, though, was a part of the parietal lobe, which contributes to spatial perception and orientation in both humans and other mammals. In dance, spatial cognition is primarily kinesthetic: you sense the positioning of your torso and limbs at all times, even with your eyes shut, thanks to the muscles' sensory organs. These organs index the rotation of each joint and the tension in each muscle and relay that information to the brain, which generates an articulated body representation in response. Specifically, we saw activation in the precuneus, a parietal lobe region very close to where the kinesthetic representation of the legs resides. We believe that the precuneus contains a kinesthetic map that permits an awareness of body positioning in space while people navigate through their surroundings. Whether you are waltzing or simply walking a straight line, the precuneus helps to plot your path and does so from a body-centered or "egocentric" perspective.

Next we compared our dance scans to those taken while our subjects performed tango steps in the absence of music. By eliminating brain regions that the two tasks activated in common, we hoped to reveal areas critical for the synchronization of movement to music. Again this subtraction removed virtually all the brain's motor areas. The principal difference occurred in a part of the cerebellum that receives input from the spinal cord. Although both conditions engaged this area—the anterior vermis—dance steps synchronized to music generated significantly more blood flow there than self-paced dancing did.

Albeit preliminary, our result lends credence

TAMI TOLPA; PETER McBRIDE *Aurora Photos* (dancers) to the hypothesis that this part of the cerebellum serves as a kind of conductor monitoring information across various brain regions to assist in orchestrating actions [see "Rethinking the Lesser Brain," by James M. Bower and Lawrence M. Parsons; Scientific American, August 2003]. The cerebellum as a whole meets criteria for a good neural metronome: it receives a broad array of sensory inputs from the auditory, visual and somatosensory cortical systems (a capability that is necessary to entrain movements to diverse stimuli, from sounds to sights to touches), and it contains sensorimotor representations for the entire body.

Unexpectedly, our second analysis also shed light on the natural tendency that humans have to tap their feet unconsciously to a musical beat. In comparing the synchronized scans with the self-paced ones, we found that a lower part of the auditory pathway, a subcortical structure called the medial geniculate nucleus (MGN), lit up only during the former set. At first we assumed that this result merely reflected the presence of an auditory stimulus—namely, music—in the synchronized condition, but another set of control scans ruled out this interpretation: when our subjects listened to music but did not move their legs, we detected no blood flow change in the MGN.

Thus, we concluded that MGN activity related specifically to synchronization and not simply listening. This finding led us to postulate a "low road" hypothesis that unconscious entrainment occurs when a neural auditory message projects directly to the auditory and timing circuits in the cerebellum, bypassing high-level auditory areas in the cerebral cortex.

So You Think You Can Dance?

Other parts of the brain engage when we watch and learn dance movements. Beatriz Calvo-Merino and Patrick Haggard of University College London and their colleagues investigated whether specific brain areas become active preferentially when people view dances they have mastered. That is, are there brain areas that

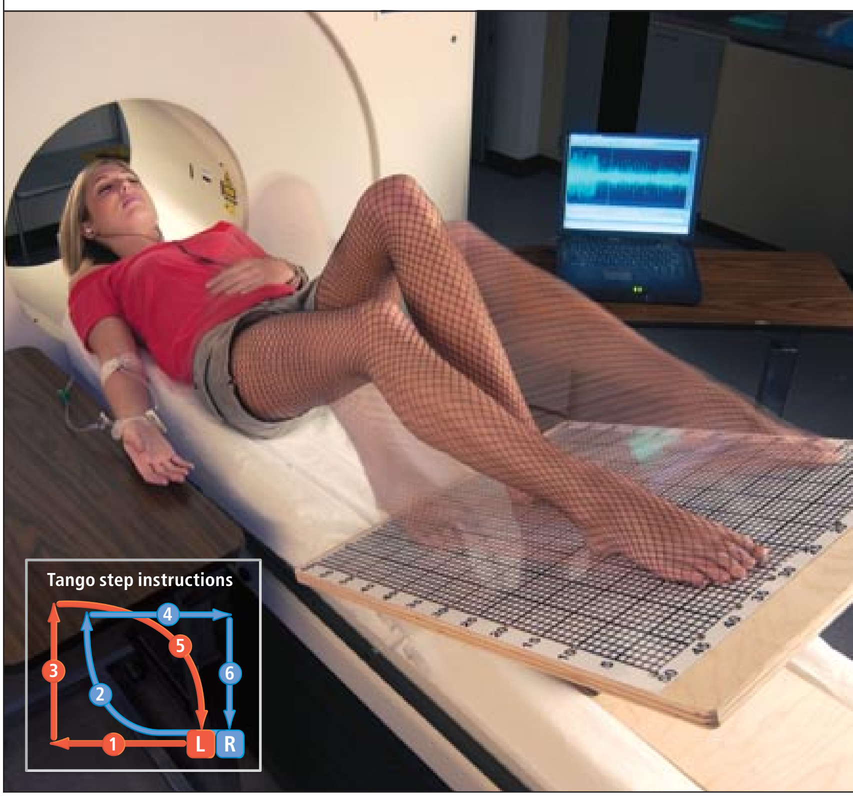
[THE AUTHORS]

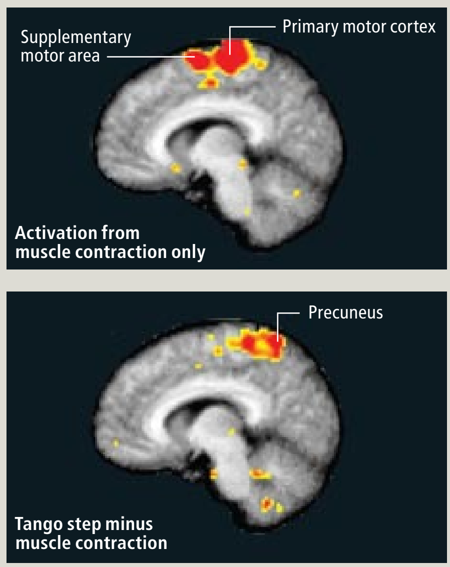
Steven Brown (*left*) is director of the NeuroArts Lab in the department of psychology, neuroscience and behavior at McMaster University in Ontario. His research focuses on the neural basis of human communication, including speech, music, gesture, dance and emotion. **Lawrence M. Parsons** (*right*) is a professor in the department of psychology at the University of Sheffield in England, where his research includes studying the function of the cerebellum and the neuroscience of dueting, turn-taking in converstaion and deductive inference.

[EXPERIMENTAL SETUP]

FANCY FOOTWORK

To identify brain areas important to dance, the authors had amateur tango dancers lie flat inside a PET scanner. The device held their heads stationary, but they were able to listen to tango music through headphones and move their legs along an inclined surface (*photograph*).





In one such experiment, the machine scanned the brain under two different conditions: when the dancers flexed their leg muscles in time to the music but did not move their limbs and when the subjects performed a basic tango box step (*inset*) with their legs, again in time to the music. When the authors subtracted brain activity caused by muscle contraction (*top scan*) from the tango scans, what remained "lit" was a part of the parietal lobe known as the precuneus (*bottom scan*).

COURTESY OF STEVEN BROWN (*Brown*); COURTESY OF LAWRENCE M. PARSONS (*Parsons and subject in scanner*); LUCY READING-IKKANDA (*illustration*); FROM "THE NEURAL BASIS OF DANCE," BY STEVEN BROWN ET AL., IN *CEREBRAL CORTEX*, VOL. 16, NO. 8; 2006 (*brain scans*)

BALLET FOR BETTER BALANCE?

Roger W. Simmons of San Diego State University has found that, when thrown off balance, classically trained ballet dancers right themselves far more quickly than untrained subjects, thanks to a significantly faster response to the disturbance by nerves and muscles. As the brain learns to dance, it also apparently learns to update feedback from the body to the brain more quickly.

switch on when ballet dancers watch ballet but not, say, capoeira (an Afro-Brazilian martial art stylized as a dance and performed to music)?

To find out, the team took functional magnetic resonance imaging scans of ballet dancers, capoeira dancers and nondancers as they viewed three-second, silent video clips of either ballet or capoeira movements. The researchers found that expertise had a major influence on the premotor cortex: activity there increased only when subjects viewed dances that they themselves could execute. Other work offers a likely explanation. Investigators have found that when people watch simple actions, areas in the premotor cortex involved in performing those actions switch on, suggesting that we mentally rehearse what we see—a practice that might help us learn and understand new movements. Researchers are examining how widely humans rely on such imitation circuits.

In follow-up work, Calvo-Merino and her colleagues compared the brains of male and female ballet dancers as they watched video clips of either male or female dancers performing gender-specific steps. Again, the highest activity levels in the premotor cortex corresponded to men viewing the male-only moves and to women viewing the female-only moves.

The ability to rehearse a movement in your mind is indeed vital to learning motor skills. In 2006 Emily S. Cross, Scott T. Grafton and their colleagues at Dartmouth College considered whether imitation circuits in the brain increase their activity as learning takes place. Over the course of several weeks, the team took weekly functional MRI scans of dancers as they learned a complex modern dance sequence. During the scans, subjects viewed five-second clips that exhibited either the movements they were mastering or other, unrelated steps. After each clip, the subjects rated how well they thought they could execute the movements they saw. The results affirmed those of Calvo-Merino and her colleagues. Activity in the premotor cortex increased during training and was indeed correlated to the subjects' assessments of their ability to perform a viewed dance segment.

Both investigations highlight the fact that learning a complex motor sequence activates, in addition to a direct motor system for the control of muscle contractions, a motor-planning system that contains information about the body's ability to accomplish a specific movement. The more expert people become at some motor pattern, the better they can imagine how that pattern feels and the more effortless it probably becomes to carry out.

As our research shows, however, the ability to simulate a dance sequence—or tennis serve or golf swing—in the mind is not simply visual, as these studies might suggest; it is kinesthetic as well. Indeed, true mastery requires a muscle sense, a motor image, as it were, in the brain's motion-planning areas of the movement in question.

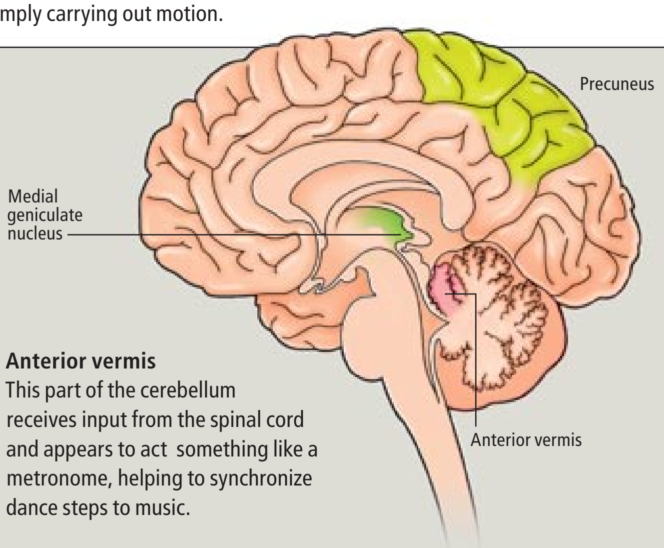
Shake, Rattle and (Social) Role

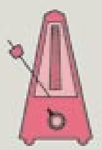
Perhaps the most fascinating question for neuroscientists to explore is why people dance in the first place. Certainly music and dance are closely related; in many instances, dance generates sound. Aztec *danzantes* in Mexico City wear leggings containing seeds from the ayoyotl tree, called *chachayotes*, which make a sound with every step. In many other cultures, people put noise-making objects—from taps to castanets to beads—on their bodies or clothes while they dance. In addition, dancers frequently clap, snap

[THE RESULTS]

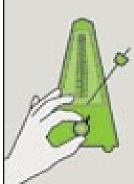
MENTAL CHOREOGRAPHY

The authors found that the following brain regions contribute to dance in ways that go beyond simply carrying out motion.





Anterior vermis
This part of the cerebellum receives input from the spinal cord and appears to act something like a metronome, helping to synchronize dance steps to music.



Medial geniculate nucleus
A stop along the lower auditory pathway, this area appears to help set the brain's metronome and underlies our tendency to unconsciously tap our toes or sway to music. We react unconsciously because the region connects to the cerebellum, communicating information about rhythm without "speaking" to higher auditory areas in the cortex.

Precuneus
Containing a sensory-based map of one's own body, the precuneus helps to plot a dancer's path from a body-centered, or egocentric, perspective.

TAMI TOLPA; NANCY BROWN *Getty Images* (*dancer's feet*)

AZTEC *DANZANTES* in Mexico City wear leggings containing seeds called *chachayotes* (*detail*), which rattle with each step. In many cultures, dancers attach noise-making objects to their bodies or clothes. Dance and music most likely evolved together as ways of generating rhythm. Unlike music, though, dance can convey ideas clearly and probably functioned as an early form of language.

KEVIN FLEMING *Corbis (dancers)*; DAVID MCNEW *Getty Images (detail)*

and stomp. As a result, we have postulated a "body percussion" hypothesis that dance evolved initially as a sounding phenomenon and that dance and music, especially percussion, evolved together as complementary ways of generating rhythm. The first percussion instruments may well have been components of dancing regalia, not unlike Aztec *chachayotes*.

Unlike music, however, dance has a strong capacity for representation and imitation, which suggests that dance may have further served as an early form of language. Indeed, dance is the quintessential gesture language. It is interesting to note that during all the movement tasks in our study, we saw activation in a region of the right hemisphere corresponding to what is known as Broca's area in the left hemisphere. Broca's area is a part of the frontal lobe classically associated with speech production. In the past decade research has revealed that Broca's area also contains a representation of the hands.

This finding bolsters the so-called gestural theory of language evolution, whose proponents argue that language evolved initially as a gesture system before becoming vocal. Our study is among the first to show that leg movement activates the right-hemisphere homologue to Broca's area, which offers more support for the idea that dance began as a form of representational communication.

What role might the homologue to Broca's area have in enabling a person to dance? The answer does not appear to involve speech directly. In a 2003 study Marco Iacoboni of the University of California, Los Angeles, and his colleagues applied magnetic brain stimulation to disrupt function in either Broca's area or its homologue. In both cases, their subjects were then less able to imitate finger movements using their right hand. Iacoboni's group concluded that these areas are essential for imitation, a key ingredient in learning from others and in spreading culture. We have another hypothesis as well. Although our study did not involve imitative movements per se, dancing the tango and copying finger actions both demand that the brain correctly order series of interdependent movements. Just as Broca's area helps us to correctly string together words and phrases, its homologue may serve to place units of movement into seamless sequences.

We hope that future neuroimaging studies will provide fresh insight into the brain mechanisms behind dance and its evolution, which is highly intertwined with the emergences of both language and music. We view dance as a marriage of the representational capacity of language and the rhythmicity of music. This interaction allows people not only to tell stories using their bodies but to do so while synchronizing their movements with others' in a way that fosters social cohesion. ■

➥ MORE TO EXPLORE

Action Observation and Acquired Motor Skills: An fMRI Study with Expert Dancers. Beatriz Calvo-Merino, Daniel E. Glaser, Julie Grèzes, Richard E. Passingham and Patrick Haggard in *Cerebral Cortex,* Vol. 15, No. 8, pages 1243–1249; August 2005.

Building a Motor Simulation De Novo: Observation of Dance by Dancers. Emily S. Cross, Antonia F. de C. Hamilton and Scott T. Grafton in *Neuroimage,* Vol. 31, No. 3, pages 1257–1267; July 1, 2006.

The Neural Basis of Human Dance. Steven Brown, Michael J. Martinez and Lawrence M. Parsons in *Cerebral Cortex,* Vol. 16, No. 8, pages 1157–1167; August 2006.

Seeing or Doing? Influence of Visual and Motor Familiarity in Action Observation. Beatriz Calvo-Merino, Daniel E. Glaser, Julie Grèzes, Richard E. Passingham and Patrick Haggard in *Current Biology,* Vol. 16, No. 19, pages 1905–1910; October 10, 2006.

Simple Groups at Play

A new set of puzzles inspired by Rubik's Cube offers puzzle lovers the chance to get acquainted with the secret twists and turns of mathematical entities called sporadic simple groups

By Igor Kriz and Paul Siegel

KEY CONCEPTS

- Success in "solving" Rubik's Cube depends on discovering short sequences of moves that accomplish limited goals.
- But the strategy is so successful that the authors yearned for puzzles whose solutions would require novel tactics.
- Basing their work on the mathematical theory of groups so well illustrated by Rubik's Cube, the authors have devised three new games that challenge today's generation of puzzle lovers with the complexities of "sporadic simple groups."

—The Editors

Millions of people have been perplexed at one time or another by Rubik's Cube, a fascinating puzzle that took the world by storm in the 1980s. If you somehow missed the puzzle—or the 1980s—the cube is a plastic gizmo that appears to be made up of 27 small cubes, or "cubies," stacked into a larger cube, three cubies to an edge. Each of the six square faces of the larger cube is colored in one of six eye-catching colors—typically blue, green, orange, red, yellow or white. We said the cube *appears* to be a stack of cubies, but appearances here are deceptive. An ingenious mechanism, invented in 1974 by a Hungarian teacher named Ernő Rubik (and, independently, in 1976 by a Japanese engineer named Terutoshi Ishige), enables any of the six square faces of the large cube to be twisted about the center of that face [*see box on page 86*]. Twist the faces in some random sequence five or six times, and you have a cube so scrambled that only an expert—a cubemeister—can restore order. The object of the puzzle is to put an arbitrarily scrambled cube back into its original state, one solid color per face, thereby "solving" the cube.

Rubik's Cube, Rubik's polyhedra and all the many knockoffs that have appeared in the cube's wake are known as permutation puzzles because they are based on moves that rearrange, or permute, the puzzle pieces (the cubies, in the case of Rubik's Cube). The object in each case is to restore some scrambled arrangement of the pieces to some predetermined order, often their initial, "virgin" configuration. Permutation puzzles are closely related to a mathematical entity called a permutation group, the set of all the sequences of allowable moves that lead to distinct arrangements of the objects in the puzzle.

In mathematics, a group can be understood as a generalization of ordinary arithmetic. The positive and negative integers 0, ±1, ±2, and so on, together with the operation of addition for

MATT COLLINS

combining them, form a group. But groups can be made up of many other kinds of entities as well—the rotations and reflections of physical objects, the various kinds of permutations that can be applied to sets of letters or things, the groupings of numbers called square matrices, and so forth—as long as the group includes some operation for combining the entities in such a way that the combinations, too, are members of the group.

In addition to its interest within pure mathematics, the theory of groups also has powerful applications outside the discipline, in such fields as crystallography, elementary particle physics, string theory and even in telecommunications. So it can be challenging as well as scientifically important for students and working scientists to gain familiarity with the ways that groups behave. Puzzling out a solution to Rubik's Cube has turned out to be a terrific way for people to get a feel for the ways that the elements of certain kinds of abstract groups combine.

But once people reach that level of mastery with the cube, they often find that their solution strategies are equally effective for solving virtually all the copycat permutation puzzles that it inspired. And, frankly, at that point this kind of permutation puzzle begins to lose its thrill. At least that was our experience with the cube. But we also knew there were good mathematical reasons for our disappointment. All the cubelike puzzles represent groups of a certain general kind, and so they all yield to the same general kinds of attack. Yet those groups by no means exhaust the mathematical diversity of the concept of a group.

What we wanted for educational purposes was an entertaining way to develop people's intuitions for groups entirely unlike the ones represented by the cube. And what we wanted as puzzle fans was a new set of puzzles whose solutions require a substantially different strategy from that of Rubik's Cube and its relatives. So we made the natural connection: we were able to develop three new puzzles based on groups known as sporadic simple groups, whose properties are both remarkable and not well known except to specialists. Happily, the experiences of our colleagues show that anyone who can learn to solve Rubik's Cube can gain an equally substantial understanding of these sporadic simple groups by doing our puzzles. But more, these puzzles are challenging in the sense that they do not yield to the methods that work with Rubik's Cube—and we think they are a lot of fun. Readers who want to get their hands on them right away can download them [see "On the Web," on page 89].

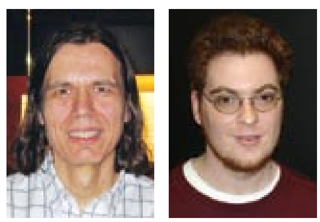
Puzzles and Their Groups

To solve the new puzzles, it is useful to understand something about the sporadic simple groups from which they are constructed, as well as how they differ from the group represented by Rubik's Cube: "Rubik's group." Groups can be infinite or finite in size. The additive group of integers we mentioned earlier obviously has infinitely many members. But the number of elements in Rubik's group is finite, even though the

ANIMATED NUMBERS perform an imagined dance as they rearrange themselves according to the "merge" move in the authors' new "M_{12}" puzzle—one of three "sporadic simple" puzzles the two have created.

COURTESY OF IGOR KRIZ (*Kriz*); COURTESY OF PAUL SIEGEL (*Siegel*)

[THE AUTHORS]

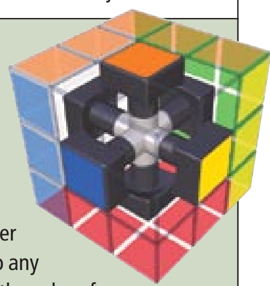


Igor Kriz (*left*) is a professor of mathematics at the University of Michigan at Ann Arbor, where he focuses on algebraic topology and mathematical physics. He earned his doctorate in mathematics from Charles University in Prague. He also enjoys playing the piano and the organ. Paul Siegel (*right*) did this work as an undergraduate at the University of Michigan. He is pursuing a Ph.D. in mathematics at Pennsylvania State University.

[PUZZLE TACTICS I]

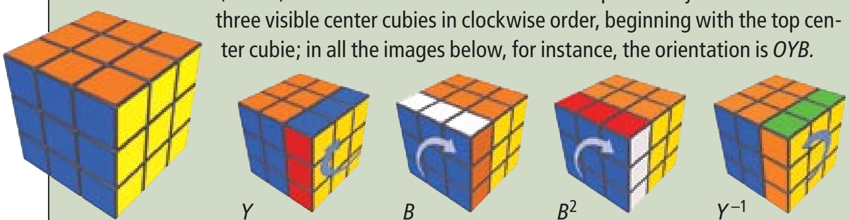
RUBIK'S CUBE CODED

Solving the authors' new puzzles builds on techniques developed for the study of mathematical entities called groups. One essential technique from group theory is specifying a simple, unambiguous system for writing down the elements of the group and how they combine.



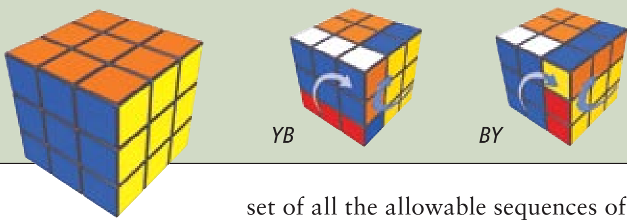
WRITING IT DOWN

Rubik's Cube represents a group whose elements are the moves—the twists you can make of each face of the cube—and whose combination rule might be called the "and then" operation: "make one twist *and then* make another." The mechanism depicted in the illustration at the right shows that no matter how the cube is scrambled, the small pieces, or cubies, at the center of each face do not move (except to rotate about their centers). So any move for solving the cube can be represented by the first letter of the color of the center cubie—*B*lue, *G*reen, *O*range, *R*ed, *Y*ellow or *W*hite—plus some way of stating how much of a twist the move involves. By itself, each letter indicates that the corresponding face is to be turned 90 degrees clockwise—looking "down" on the face from outside the cube (moves *Y* and *B* in the diagram below). A superscript indicates other kinds of turns. B^2 turns the blue face 180 degrees; Y^{-1} turns the yellow face 90 degrees counterclockwise (*below*). The orientation of the cube can be specified by the colors of the three visible center cubies in clockwise order, beginning with the top center cubie; in all the images below, for instance, the orientation is *OYB*.



HINT: ORDER COUNTS

The sequence of moves is critical to solving the cube, so the notation must capture the differences. The composite moves *YB* and *BY* do not take a given starting arrangement of the cubies to the same final configuration.



set of all the allowable sequences of moves of Rubik's Cube is infinite. The reason is that if two sequences of moves lead from the same starting arrangement of cubies to the same end point, the sequences are regarded as equivalent. In Rubik's Cube the number of distinct configurations of cubies is astronomical—about 4×10^{19}, or 43,252,003,274,489,856,000, to be precise—so the number of elements, or distinct combinations of moves in the group represented by the cube, is gigantic but finite.

In spite of that vast "space" of moves, it is not hard to devise a solution to the cube by following a few general hints. You need a pencil, paper and one Rubik's Cube, preferably unscrambled. Your aims are twofold: First, you want some convenient way of recording your moves [*see box above*]. Second, you want to discover various short sequences of moves that you can write down for accomplishing specific tasks: exchanging certain pairs of corner cubies or edge cubies, for instance [*see box on opposite page*]. The idea is to combine the sequences systematically to solve a scrambled cube.

It turns out that this systematic approach, begun by trial and error, almost invariably leads to useful sequences that give you enough flexibility to solve the cube. Roughly speaking, the reason is that the basic algebraic components of Rubik's group are the so-called symmetric groups, which are groups of all possible permutations of a given number of objects, and their close relatives the alternating groups, each of which contains half the elements of the corresponding symmetric group. Thus, the symmetric group S_3 contains all 3! ($1 \times 2 \times 3$), or six, possible permutations of three objects [*see box on page 88*]; its relative, the alternating group A_3, has three elements. Among the symmetric groups related to Rubik's group are the symmetric group S_8 (all the 8!, or 40,320, ways the eight corner cubies can be rearranged) and the symmetric group S_{12} (all the 12!, or 479,001,600, ways the 12 edge cubies can be rearranged).

"Atoms" of Symmetry

Our puzzles, too, are permutation puzzles, but each of them is based on a so-called sporadic simple group. To understand what a sporadic simple group is, begin with the concept of a subgroup. Suppose you are allowed to twist only the blue and yellow faces of Rubik's Cube. Under that restriction you will never be able to move the side cubie colored green and white. Hence, the number of distinct sequences of restricted moves is smaller than the number of elements in Rubik's group as a whole. Whenever all the combinations of some subset of the moves in a puzzle group are also moves within the subset, the subset is called a subgroup. Beyond that point the concept of a simple group is somewhat technical; suffice it to say that a simple group is a group that contains no "proper, normal" subgroups [*for a detailed explanation, see box on page 88*].

The term "simple" as it is applied in group theory may be one of the greatest misnomers in the history of mathematics. The simple groups have turned out to include some of the most complex entities known to mathematicians. Yet they are simple in the sense that they are the building blocks, or "atoms," of group theory. In a way, the simple groups are also like the prime numbers, numbers divisible only by themselves

GEORGE RETSECK (*cubes*)

and by 1 (2, 3, 5, 7, 11, and so on). Every finite group can be uniquely "decomposed" into simple groups, just as any whole number can be factored into primes.

All the finite simple groups have been identified and classified. They were discovered between the 1860s and 1980, and the classification was done mostly between the late 1940s and the early 1980s (with some more recent corrections), involving the work of hundreds of mathematicians. Reports of discoveries of simple groups and the proof that the final list was complete consumed more than 10,000 pages in professional mathematics journals, distributed across some 500 articles. Mathematicians are still working on a simpler version of that proof, which could clarify their understanding of the simple groups. But the proof already in hand shows that there are 18 families of finite simple groups—each family an infinite collection of specific kinds of groups—and 26 so-called sporadics that are oddballs, essentially mathematical entities unto themselves. There are no others.

Sporadic Simple Puzzles

We constructed puzzles based on the three sporadic simple groups known as M_{12}, M_{24} and Co_1. Those puzzles, like Rubik's Cube, are permutation puzzles, but the permutations that represent sporadic simple groups are far more restrictive about the allowed permutations than the symmetric groups are. Thus, in our puzzles many arrangements of numbers are inaccessible, no matter how many moves one makes.

As we noted earlier, the strategy that works for solving the cube and other puzzles based on symmetric groups does not work for our new puzzles. But other strategies can be developed from only small hints about the groups.

The simplest of our three puzzles is M_{12}, based on the sporadic simple group of the same name. The M_{12} group is one of the first five sporadic simple groups ever discovered; all five were found in the 1860s by French mathematician Émile Mathieu and are dubbed Mathieu groups. The would-be puzzle solver confronts a specially scrambled sequence of the numbers 1 through 12, arranged in a row. Only two moves are allowed, though they can be applied any number of times in any sequence [*see box on page 89*]. The object of the puzzle is to put the scrambled arrangement back into ordinary numerical order (1, 2, 3, . . ., 12).

We will give just one hint to readers bold enough to take on our challenge. In the puzzle (and in the group M_{12}), it is possible to move any five of the numbers to any five of the 12 positions in the row. Once that is done, all the remaining numbers fall into position; the puzzle is solved. The reason is that the group M_{12} has $12 \times 11 \times 10 \times 9 \times 8$, or 95,040, permutations, which happens to be exactly the number of ways of selecting any five of the 12 numbers and placing each of them somewhere in the sequence. (The first number can take any one of the 12 positions, the second any one of the remaining 11 positions, and so on.) The fact that the entire permutation is specified by fixing the positions of five numbers implies that it is pointless to search for a sequence of moves that would shift only a few numbers. Except for the so-called dummy, or null, move, which leaves any arrangement just as it is, every move must leave fewer than five numbers fixed. In other words, every

THREE PUZZLES, SO MANY MOVES

- M_{12} puzzle (based on Mathieu group M_{12}): 95,040 permutations
- M_{24} puzzle (based on Mathieu group M_{24}): 244,823,040 permutations
- Dotto puzzle (representing Conway group Co_0): 8,315,553,613,086,720,000 permutations

[PUZZLE TACTICS II]

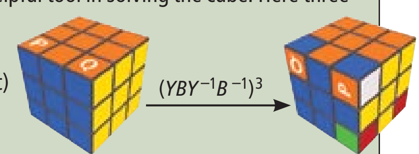
RUBIK'S CUBE DECODED

Classic permutation puzzles such as Rubik's Cube, whose object is to rearrange the pieces into some target configuration, can usually be solved by following a two-step strategy.

STEP 1

By trial and error, select a short, random sequence of moves, such as $YBY^{-1}B^{-1}$ (this notation is explained in the box on the opposite page).

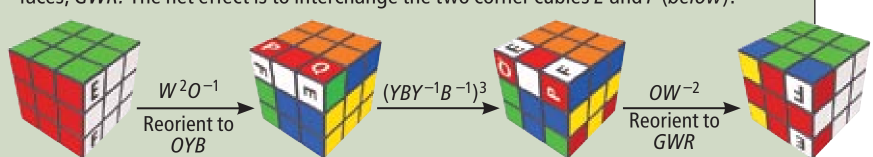
Repeat the random sequence several times. Often that will lead to an arrangement in which only a few cubies have been moved—a helpful tool in solving the cube. Here three repetitions, or $(YBY^{-1}B^{-1})^3$, switch two pairs of corner cubies: the pair bordering the blue and orange faces (cubies labeled *P* and *Q* at the right) and the pair bordering the yellow and red faces.



Virgin cube (*OYB* orientation)

STEP 2

Modify and generalize the useful move you found. For example, to interchange the pair of corner cubies bordering the red and white faces (cubies labeled *E* and *F* on a "virgin" cube shown below, for clarity, in orientation *GWR*), look for a move that "sets up" your "useful move." Applying the short setup sequence W^2O^{-1} moves corner cubies *E* and *F* into positions *P* and *Q* (for clarity, the cube faces are reoriented from *GWR* to *OYB*). You can now apply the useful move $(YBY^{-1}B^{-1})^3$, undo the setup sequence by making the opposite moves in reverse order, OW^{-2}, and restore the initial orientation of the cube faces, *GWR*. The net effect is to interchange the two corner cubies *E* and *F* (*below*).



Virgin cube (*GWR* orientation)

A similar setup sequence can be found for moving any pair of corner cubies to one of the two pairs interchanged by $(YBY^{-1}B^{-1})^3$. You can thus construct a custom move for interchanging any pair of corner cubies. Proceeding in the same way with other random sequences gives enough flexibility to solve the cube and any other classic permutation puzzle.

GEORGE RETSECK (*cubes*)

nontrivial sequence of moves must displace at least eight of the 12 numbers.

Puzzles Not for the Faint of Heart

Our second puzzle, M_{24}, includes 23 numbers arrayed in a circle, as if on the face of a clock, and a 24th number placed just outside the circle at 12 o'clock. As in the M_{12} puzzle, just two moves are allowed [*see box on opposite page*]. In principle, the M_{24} puzzle could be manufactured from real parts rather than just represented by a computer: the circle of 23 numbers could

[BASICS]

WHAT IS A SPORADIC SIMPLE GROUP?

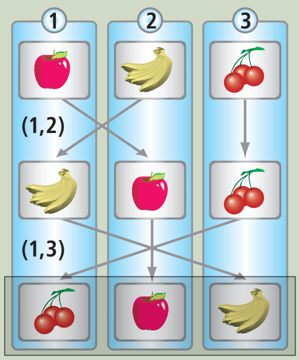
All three new puzzles represent sporadic simple groups of permutations. Making sense of that statement takes a few preliminaries.

NOTATION, NOTATION, NOTATION

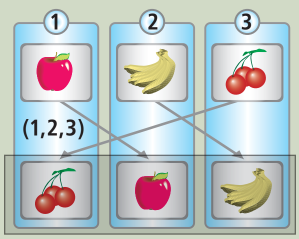
The "symmetric" group S_n is the group of all possible permutations, or rearrangements, of *n* objects or symbols in a row. The symmetric group S_3, for instance, is the set of the six distinct permutations that give rise to the six possible arrangements of three different objects. A group of permutations always includes the "dummy" permutation, written (1), that does nothing.

The permutation (1,2) interchanges the objects in the first and second positions (*right*).

The permutation (1,3) interchanges the objects in the first and third positions. Applying (1,3) to the result of (1,2), written (1,2) ∘ (1,3), gives the arrangement at the right.



Combining these two permutations is equivalent to applying just one permutation, written (1,2,3). The notation is shorthand for cycling the objects from the first position to the second, from the second position to the third, and from the third position to the first.



"MULTIPLICATION" IS THE NAME OF THE GAME

The table for the six permutations of three objects shows how all 36 pairs of elements in S_3 combine. The dummy permutation (1) acts like the number 1 in an ordinary multiplication table. Note that every "product" permutation in the table is equal to one of the six "multiplier" permutations (*white boxes*), a property of all groups known as closure.

	∘ ("and then")	Second, do this permutation					
		(1)	(1,2,3)	(1,3,2)	(1,2)	(1,3)	(2,3)
First, do this permutation	(1)	(1)	(1,2,3)	(1,3,2)	(1,2)	(1,3)	(2,3)
	(1,2,3)	(1,2,3)	(1,3,2)	(1)	(2,3)	(1,2)	(1,3)
	(1,3,2)	(1,3,2)	(1)	(1,2,3)	(1,3)	(2,3)	(1,2)
	(1,2)	(1,2)	(1,3)	(2,3)	(1)	(1,2,3)	(1,3,2)
	(1,3)	(1,3)	(2,3)	(1,2)	(1,3,2)	(1)	(1,2,3)
	(2,3)	(2,3)	(1,2)	(1,3)	(1,2,3)	(1,3,2)	(1)

What Happens in a Subgroup, Stays in a Subgroup

Every product of the three permutations in the orange region of the table is equal to one of those same three permutations. Because of that closure property, the three permutations also form a group: a so-called subgroup of the bigger group S_3.

You Can Always Undo

For every permutation in the left column of the table, one of the product entries in its row is (1), the dummy permutation. In the same column as that (1), the multiplier heading the column is called the inverse of the first permutation. In short, every permutation *g* has an inverse, denoted g^{-1}. For example, the inverse of (1,2,3), written $(1,2,3)^{-1}$, is (1,3,2), because (1,2,3) ∘ (1,3,2) is equal to (1); (1,2) is its own inverse, written $(1,2)^{-1}$, because, as the table shows, (1,2) ∘ (1,2) = (1).

PUTTING IT ALL TOGETHER

A simple group is a group with no "proper, normal" subgroups. Every group has at least two subgroups, itself and the subgroup whose only member is (1); a proper subgroup is any other subgroup that may exist.

So What Is Normal?

Pick any permutation in the multiplication table, say, (1,2), and "multiply" it by any permutation in the orange-tinted subgroup, say, (1,2,3).

(1,2) ∘ (1,2,3) = (1,3)

Multiply the result by the inverse of the first permutation, here (1,2):

(1,3) ∘ (1,2) = (1,3,2)

In short: (1,2) ∘ (1,2,3) ∘ $(1,2)^{-1}$ = (1,3,2)

If the result of every triple product defined in the same way lies within the subgroup, the subgroup is normal. Here the end product (1,3,2) does indeed lie in the orange-tinted subgroup.

Okay, That's Simple. What's Sporadic?

Most simple groups have been classified into simple-group families with an infinite number of members. But 26 of them are oddballs that belong to no such families, nor do they have much in common. To avoid the term "miscellaneous," mathematicians call them sporadic.

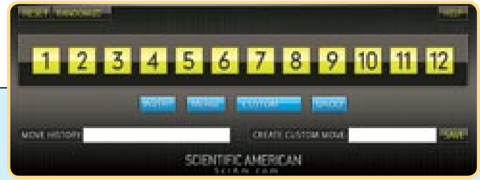
—Peter Brown, staff editor

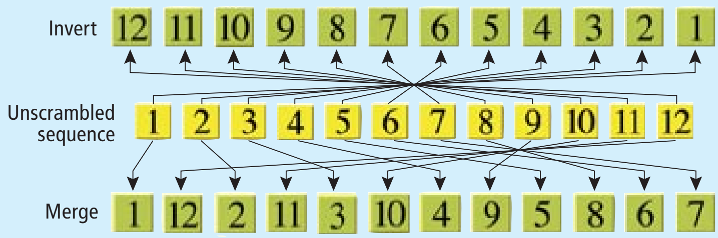
JOHNNY JOHNSON

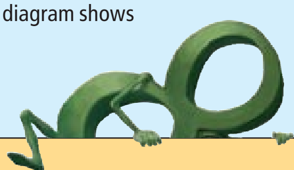
[SCREEN SHOTS]

WHAT YOU'LL FIND ONLINE

Mathieu puzzle M_{12}, which represents the sporadic simple group M_{12}, was designed by the authors to be played on the Internet. The puzzle begins with a scrambled version of the numbers 1 through 12. The object is to unscramble them using combinations of just two moves, both conveniently executed at the click of a button. The diagram shows the effect of each move on the unscrambled numbers.







A second Mathieu puzzle, M_{24}, represents the sporadic simple group M_{24}. In the unscrambled state the numbers 1 through 23 are arranged in a clocklike circle, and a 0 is placed just outside the circle at 12 o'clock. As with the M_{12} puzzle, the object is to restore the unscrambled order from a scrambled state. The M_{24} puzzle also has two moves. One move rotates the circle one "notch," sending the number in position 1 to position 2, the number in position 2 to 3, and so forth. The number in position 23 is sent to position 1, and the number outside the circle does not move. The second move simply switches the pairs of numbers that occupy circles having the same color.

be moved by a rotating device, and a system of gears could swap pairs of numbers as dictated by the moves.

The group of permutations generated by the two moves of M_{24} is the Mathieu group M_{24}. Like M_{12}, M_{24} is "five-transitive": with some combination of the two moves, it is possible to manipulate the arrangement until any five of the 24 numbers are positioned in any five of the 24 positions. Because of five-transitivity, our hint for solving the M_{12} puzzle helps in solving M_{24} as well: devise moves that return the numbers 1 through 5 to their proper positions without disturbing the numbers already in place. But this time the solver is not quite done. The group M_{24} has $24 \times 23 \times 22 \times 21 \times 20 \times 48$, or 244,823,040, elements; thus, even after the numbers 1 through 5 are returned to their proper places, the other 19 numbers can still be distributed around the circle in 48 different ways.

Dotto, our final puzzle, represents the Conway group Co_0, published in 1968 by mathematician John H. Conway of Princeton University. Co_0 contains the sporadic simple group Co_1 and has exactly twice as many members as Co_1. Conway is too modest to name Co_0 after himself, so he denotes the group ".0" (hence the pronunciation "dotto").

We will have to leave the details of the Dotto puzzle to our online discussion. But we can point out that both the puzzle and its underlying group have fascinating mathematical properties. The puzzle is closely related to the Leech lattice, a set of "points," or ordered lists of numbers, in a 24-dimensional space. It is known that among all sphere packings in 24-dimensional space constructed by centering 24-dimensional "spheres" on the points of a lattice, a sphere packing based on the Leech lattice is the tightest.

Of Babies and Monsters

Only four sporadic simple groups surpass Co_1 in size: the Janko group J_4, the Fischer group Fi_{24}', the Baby Monster B and the Monster M. True to its name, the Monster is the largest of them all, with some 8×10^{53} elements. It was constructed in 1980 by Robert L. Griess, Jr., of the University of Michigan at Ann Arbor as the group of transformations of a certain complicated mathematical structure in 196,884-dimensional space.

We have not tried constructing puzzles on the basis of any other sporadic simple groups—although some are surely possible. But designing any workable puzzle based on the Monster would be a serious mathematical undertaking. The reason is that it is not known whether the Monster is the permutation group of any object small enough to be visualized, although, according to one conjecture, it is the permutation group of a certain 24-dimensional curved space. A successful design of a "Monster puzzle" might bring mathematicians closer to proving this tantalizing conjecture. ■

ON THE WEB

SCI AM

All three games, M_{12}, M_{24} and Dotto, are available at **www.SciAm.com/jul2008**

[M_{12} and M_{24} have been reprogrammed by *Scientific American* to run over the Internet on any computer; Dotto is available for download only to PCs.]

➥ MORE TO EXPLORE

Metamagical Themas: The Magic Cube's Cubies Are Twiddled by Cubists and Solved by Cubemeisters. Douglas R. Hofstadter in *Scientific American,* Vol. 244, No. 3, pages 20–39; March 1981.

The Enormous Theorem. Daniel Gorenstein in *Scientific American,* Vol. 253, No. 6, pages 104–115; December 1985.

Sphere Packings, Lattices and Groups. Third edition. John Horton Conway and Neil J. A. Sloane. Springer-Verlag, 1999.

Finite Group Theory. Second edition. M. Aschbacher. Cambridge University Press, 2000.

Twelve Sporadic Groups. Robert L. Greiss, Jr. Springer Monographs in Mathematics, 2002.

For a list of the sporadic groups: **Sporadic Group.** Eric W. Weisstein in *MathWorld—A Wolfram Web Resource.* **http://mathworld.wolfram.com/SporadicGroup.html**

RYAN REID

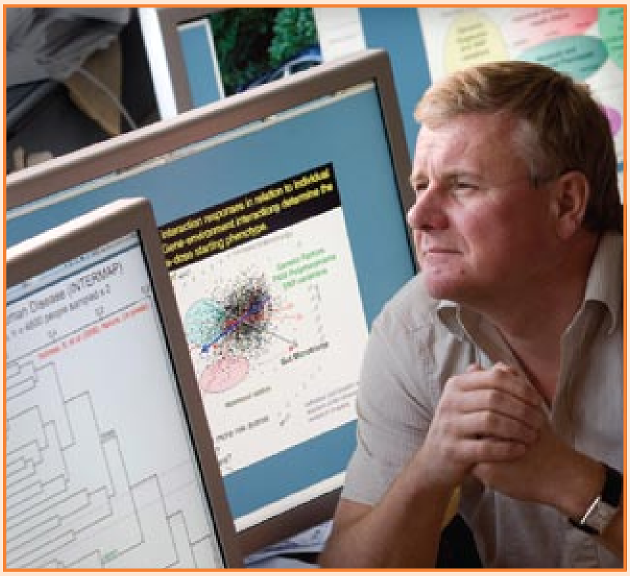
Going with His Gut Bacteria

The body and its intestinal flora produce chemicals with hidden health information, Jeremy Nicholson has found. Someday treating disease may mean treating those bacteria BY MELINDA WENNER

Jeremy Nicholson was only trying to be thorough. It was 1981, and the young biochemist was using a technique called nuclear magnetic resonance spectroscopy, which can identify chemicals based on the magnetic properties of atomic nuclei. In particular, Nicholson wanted to study how red blood cells absorb cadmium, a metal that causes cancer. Realizing that he would achieve the best results if he could mimic the cells' natural environment, he added a few drops of blood to the cells and ran the test.

"Suddenly there was a huge variety of signals that we hadn't seen before—there were these amazing sets of spectra coming out," Nicholson recalls. A sample of blood or urine contains thousands of metabolites—signatures of all the chemical reactions occurring in the body at a given time. If he could find a way to identify those chemical signatures and their significance, he reasoned, he would be able not only to better understand different diseases—based on chemical reactions that had gone awry—but also to identify early warning signs and potential interventions. That kind of science, he decided, was his kind of science.

Today the 51-year-old Nicholson is one of the world's foremost experts on the so-called metabolome, the collection of chemicals produced by human metabolism. Whereas the genome provides detailed information about a person's genetic makeup, the metabolome is a few steps down the line—it reveals how genes interact with the environment, providing a complete snapshot of a person's physical health. "The genome is really like a telephone directory without any of the names or addresses filled in. On a very basic level, it's got a lot of numbers," explains Nicholson, who now heads the department of biomolecular medicine at Imperial College London. The metabolome "helps to give value to genome information and put it in perspective."



JEREMY NICHOLSON

BACTERIAL CLUES: By analyzing the products of intestinal bacteria, Nicholson hopes to fashion new tools for diagnosis and new targets for drugs.

POPULATION BOOM: The human gut contains some 10 trillion individual bacteria in 1,000 different species.

FATHER OF DISCIPLINES: Nicholson's work has spawned two new fields: metabolomics, which studies the metabolites that cellular processes leave behind, and metabonomics, which characterizes the metabolic changes a biological system experiences in response to stressors.

GROWING ON HIM: On first noticing metabolic fingerprints that cells leave behind: "I was thinking of them as extremely annoying interferences with mammalian biochemistry. Now I'm almost becoming evangelical about the bloody things."

SION TOUHIG

But first it has to be deciphered, and that is no easy task. The job requires the analysis of blood, urine, breath and feces within large populations. For instance, to find potential chemical signatures, or biomarkers, for high blood pressure, Nicholson and his colleagues analyzed the urine of 4,630 individuals from the U.K., the U.S. and Asia and compared the urinary metabolites with blood pressure data to determine if any consistent metabolic differences exist between individuals with hypertension and those without it.

It is kind of like doing science backward: instead of making hypotheses and then devising experiments to test them, he performs experiments first and tries to decipher his results later. He must sift through the range of chemicals produced by the genes people have, the food they eat, the drugs they take, the diseases they suffer from and the intestinal bacteria they harbor.

Those bacteria in particular have become Nicholson's prime focus. They influence how our bodies break down food and drugs and may explain why food affects people differently. For instance, some people cannot derive benefit from one of soy's components because they lack the gut microbes necessary to process it. Although deciphering which metabolites come directly from our gut microbes can be difficult, in some cases it is easy—they are the chemicals that are not produced by cells or ingested in food.

Nicholson focuses on these chemicals both because little is known about them and because they appear to be highly relevant: recent research suggests that gut microbes play a crucial role in human health and disease. They help us absorb nutrients and fight off viruses and "bad" bacteria; disrupting intestinal colonies, such as with a course of antibiotics, often leads to digestive sickness. In fact, Nicholson says, "almost every sort of disease has a gut bug connection somewhere."

Perhaps the most well-known disease-causing gut organism is the bacterium *Helicobacter pylori,* which can trigger peptic ulcer. In the past few years, scientists have linked obesity to the relative abundance of two dominant intestinal bacterial phyla and found that dysfunctional intestinal bacteria are associated with nonalcoholic fatty liver disease, inflammatory bowel disease and some types of cancer. Nicholson even speculates that the organisms could play a role in neurological disorders, such as attention-deficit hyperactivity disorder, Tourette's syndrome and autism. "We have some evidence now that shows that if you mess around with the gut microbes, you mess around with brain chemistry in major ways," Nicholson remarks. He currently collaborates with microbiologists to match metabolites with specific bacteria—there are thought to be 1,000 species and more than 10 trillion bacterial cells inside us at any given time.

This identification process has only recently become possible. Although scientists have been able to extract gut bacteria from fecal samples for many years, it has been next to impossible to culture the samples afterward because they survive only in highly acidic, oxygen-free environments. Thanks to new DNA-sequencing technologies, scientists can now identify gut bacteria fairly easily, and there is growing interest in doing so: the National Institutes of Health launched its Human Microbiome Project last December with the goal of fully characterizing the human gut flora.

Once investigators can correlate metabolites with health, it may one day be possible, Nicholson says, to make urine sticks similar to those used in pregnancy tests to regularly check the fitness of our gut flora. Some companies have already begun selling food products to help keep these populations in line—with live beneficial bacteria (probiotics) or compounds that help these species grow (prebiotics), or combinations of the two (synbiotics). Unfortunately, these medications typically fall into the category of "functional foods," which means they are rarely tested in clinical trials. One exception is VSL #3, a combination of eight bacterial species sold in packet form by the Gaithersburg, Md.–based VSL Pharmaceuticals. In double-blind, placebo-controlled trials, the colonies effectively treated ulcerative colitis and irritable bowel syndrome.

LIVE-IN COMPANIONS: *Helicobacter pylori* (*red*) and other gut bacteria greatly influence health.

Many possibilities exist for bug-based drugs, and there is a strong need for them, Nicholson maintains. According to a study published by scientists at the pharmaceutical giant Pfizer, the human genome offers only about 3,000 potential drug targets, because just a subset of genes produces proteins that can be bound and modified by druglike molecules. But "there are 100 times as many genes in the microbial pool," says Nicholson, who regularly works with drug companies to better elucidate how people metabolize medicines. He is "one of a few academics I've met who's interested in the pharmaceutical industry for its problems rather than just for its cash," comments Ian Wilson, a scientist working in England for the pharmaceutical company AstraZeneca. Wilson adds that Nicholson is always full of potential solutions, referring to him as "a bubbling mass of ideas."

Because genes provide only limited information about a person's risk for disease, Nicholson dreams of a time when physicians can provide personalized health care on the metabolome. Simple blood or urine tests would detect the risk of cancer or heart disease early enough to begin preventive therapy; drugs would be tailored to each person's metabolic profile—and in many cases, they would not target our organs but our bacteria. "It opens up visions of a future that we would never have suspected even a few years ago," Nicholson says. "Many microbiologists might argue this is fanciful, but you only make huge progress in science by thinking almost the unthinkable." ■

Melinda Wenner is a freelance science writer based in New York City. A Q&A version of her interview with Nicholson is at **www.SciAm.com/jul2008**

PHOTO RESEARCHERS, INC.

Nimble Skyscrapers at Sea

By Mark Fischetti

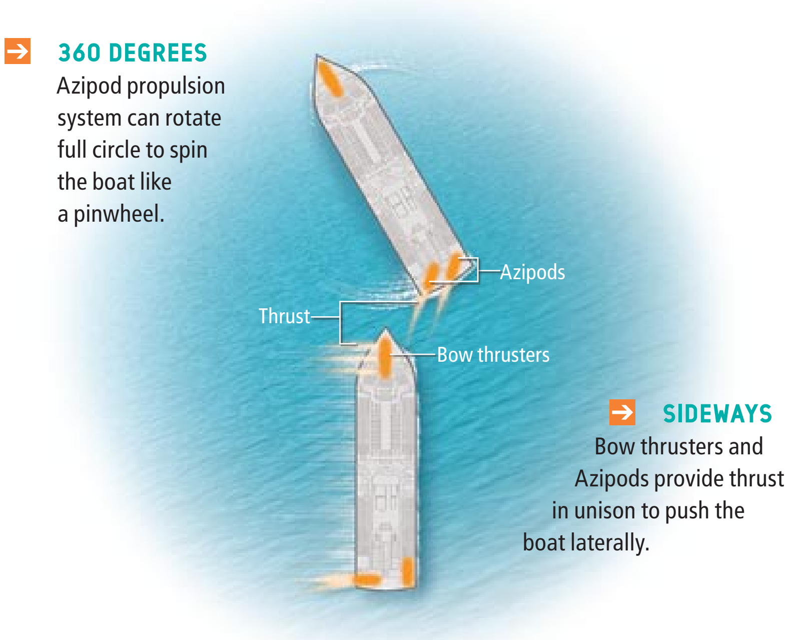
Large cruise ships typically host 1,800 passengers or more, plus 800 staff. Remarkably, many of these massive structures—three football fields long and 14 stories high—can deftly turn on a dime, spin 360 degrees, even mosey sideways.

For years big ship propulsion had a standard configuration: a propeller in the rear with a rudder behind it to steer. But increasingly, they are being equipped with an innovative propulsion system called the Azipod, made by ABB Oy in Finland. This gigantic electric motor and propeller hang underneath the back of the ship from a hefty swivel that allows the rig to rotate 360 degrees, driving the ship in any direction. Smaller bow thrusters, installed laterally under the waterline in the nose of the hull, help to push the boat from side to side near docks or obstructions.

The *Oosterdam,* owned by Holland America Line, is typical of big ocean liners. Five diesel engines, one gas turbine and two Azipods move the floating high-rise swiftly and smoothly. The power comes at a price: 90 gallons of heavy fuel oil are consumed per mile when running at moderate speed on three engines; up to 150 gallons are needed per mile when all five engines are bucking headwinds and swells at top speed. "Every day I recalculate the fuel figures and adjust operations" to maximize fuel efficiency, said Willem Dullaert, chief engineer of the *Oosterdam* when this writer was onboard earlier in the year. For example, ballast, fuel or freshwater might be pumped from tank to tank to alter how the craft rides.

"Each ship has a most economical draft," notes Cees Deelstra, Holland America's director of nautical operations. "We even consume fuel and water out of different tanks to perfect the trim." In calm seas, about two thirds of the power generated moves the ship and the rest caters to its inhabitants' desires.

The scale of equipment in the bowels of such boats is impressive. An adult can literally walk inside an engine, which occupies the volume of a suburban living room. Evaporators the size of small cars can each desalinate almost 140,000 gallons of seawater a day to provide freshwater for passengers and staff. Engines are cooled with closed-loop freshwater systems that, in turn, are cooled by adjacent closed loops of seawater. Cruise lines used to give patrons who asked brief tours of their ships' guts, but sadly, concerns about terrorism have ended the inside look on most excursions.



OOSTERDAM'S PARTICULARS

Length 934 feet	Top speed 24 knots (27.6 mph)	Fuel consumption, full throttle 150 gallons per mile
Breadth 105 feet	Maximum power 88,900 horsepower	Fuel tank capacity 863,000 gallons
Propeller span 18 feet	Freshwater production 334,000 gallons per day	Ballast tank capacity 1,730,185 gallons

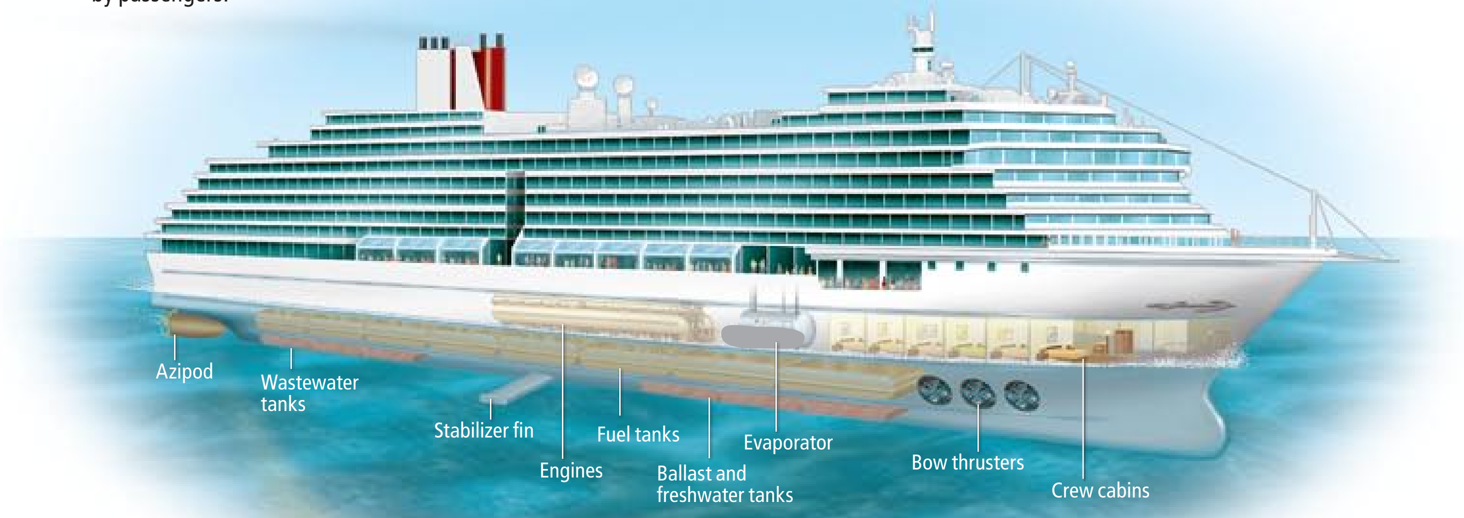
DID YOU KNOW ...

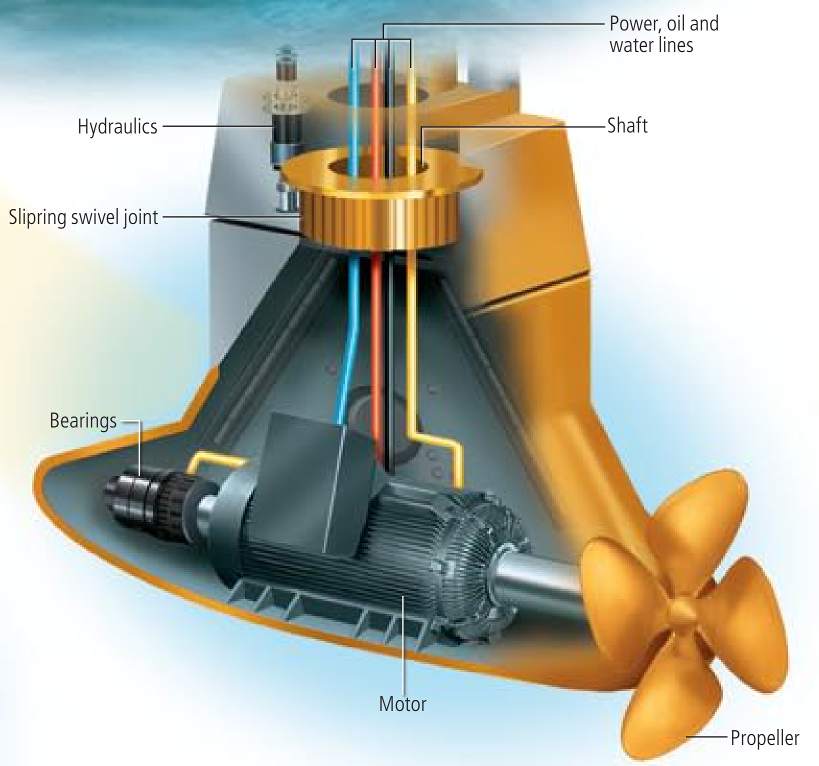
GREENER BOAT: Newer cruise ships process "graywater" from showers and sinks into clean water for various operations. So-called blackwater from toilets is also treated; cleansed water is discharged at sea, and solidified waste is brought ashore. Some operators are also experimenting with smokestack scrubbers to filter engine emissions.

LAW ON THE SEA: As soon as passengers step onto a ship, they enter into the legal system of the owner's home country. For example, the *Oosterdam* sails under the Dutch flag, so all people onboard are subject to Dutch law.

HIDDEN CREW: For a weeklong trip, the *Oosterdam* sails nine navigation officers, 17 engineers, an environmental officer, an information technology officer, an electrician, a carpenter, a locksmith, an upholsterer and a tilesetter. Passengers are pampered by 400 room stewards and 400 waitstaff—all from Indonesia and the Philippines; these employees work seven days a week for 10 months a year, sleep two to a room and move about via hidden stairways.

ENGINES, tanks and myriad mechanical systems are spread across a cruise ship's lower decks, rarely seen by passengers.





TWO STEEL FINS, 24 feet long, counteract starboard and port rolls (*shown*) caused by ocean swells.

KENT SNODGRASS *Precision Graphics*

PROPELLER is turned by an electric motor inside the Azipod, which draws current from generators powered by the ship's engines. Hydraulics can swivel the unit 360 degrees. Motor current, lubricants and cooling water pass through the swivel joint.

SEND TOPIC IDEAS *to workingknowledge@SciAm.com*

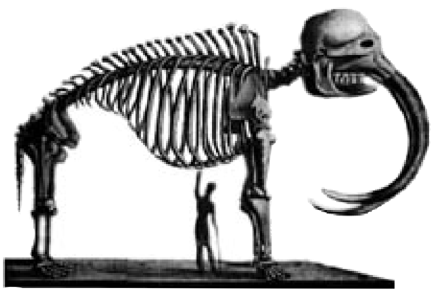
Fossils in America ▪ Science and Religion ▪ A Giant Moon

BY MICHELLE PRESS

THE LEGACY OF THE MASTODON: THE GOLDEN AGE OF FOSSILS IN AMERICA

by Keith Thomson. Yale University Press, 2008 ($35)

In the mid-1700s frontiersmen uncovered mastodon bones in present-day Kentucky. In this unique and fascinating book, Thomson, a professor emeritus of natural history at the University of Oxford, takes us from the mastodon bones through finds of many unsuspected kinds of animals—tiny ancestors of horses and camels, birds with teeth, cattlelike creatures with claws and, of course, dinosaurs. All this is fascinating, but what makes the book unique is that Thomson links the emergence of the new nation to the discovery of its fossils.

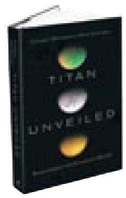


MASTODON RECONSTRUCTION in the early 1800s reversed the tusks to make the creature seem more fearsome.

Along the way, he turns up many surprising gems. American proponents of the New World, for example, were eager to prove that the native animals were larger and fiercer than those of the Old World. Thomas Jefferson and others even suggested that the recently discovered mastodon had been carnivorous. They were not without provocation: the Comte de Buffon, the great French naturalist, disparaged the fauna and flora of the Americas, going so far as to sneer that " 'in the savage, the organs of generation are small and feeble. He has no hair, no beard, no ardour for the female.' "

TITAN UNVEILED: SATURN'S MYSTERIOUS MOON EXPLORED

by Ralph Lorenz and Jacqueline Mitton. Princeton University Press, 2008 ($29.95)

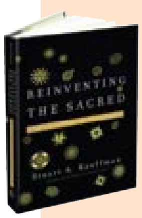


Titan, one of Saturn's roughly 50 moons, is aptly named. At 5,150 kilometers across, it is larger than Mercury. It also boasts turbulent orange skies, methane monsoons, equatorial sand seas and a polar hood. So intriguing is this moon that when NASA and the European Space Agency launched the Cassini satellite in 2004 to explore Saturn, they designed a separate probe—Huygens—that would detach and drop through Titan's haze. Lorenz, a planetary scientist, and Mitton, a science writer, vividly describe this encounter with an alien landscape; excerpts from Lorenz's log convey what it was like to be involved in the mission. "Psychologically," the authors write, "Huygens made Titan a real place—a place to which we might soon return."

EXCERPT

REINVENTING THE SACRED: A NEW VIEW OF SCIENCE, REASON AND RELIGION

by Stuart A. Kauffman. Basic Books, 2008 ($27)



Complexity theorist Kauffman acknowledges that the very notion of "reinventing" the sacred is likely to incite angry reactions from those who believe that a Creator God exists and that the sacred is an expression of His being and law. But his provocative argument for a different understanding of God is compelling:

"Is it, then, more amazing to think that an Abrahamic transcendent, omnipotent, omniscient God created everything around us … in six days, or that it all arose with no transcendent Creator God, all on its own? I believe the latter is so stunning, so overwhelming, so worthy of awe, gratitude, and respect, that it is God enough for many of us. God, a fully natural God, is the very creativity in the universe. It is this view that I hope can be shared across all our religious traditions, embracing those like myself, who do not believe in a Creator God, as well as those who do. …

"This view is not as great a departure from Abrahamic thought as we might suppose. Some Jesuit cosmologists look out into the vast universe and reason that God cannot know, from multiple possibilities, where life will arise. … Such a God is a Generator God who does not know or control what thereafter occurs in the universe. Such a view is not utterly different from one in which God is our honored name for the creativity in the natural universe itself."

NEW AND NOTABLE BIOGRAPHIES

1 **Einstein and Oppenheimer: The Meaning of Genius**
by Silvan S. Schweber. Harvard University Press, 2008 ($29.95)
Two great scientists' contrasting characters and accomplishments provide powerful insights into their lives and the scientific culture of their times.

2 **A Force of Nature: The Frontier Genius of Ernest Rutherford**
by Richard Reeves. Atlas Books/W. W. Norton, 2008 ($23.95)
This critically acclaimed historian brings to life the story of Rutherford and his team's success in splitting the atom—an act that would change the world.

3 **The Death of Sigmund Freud: The Legacy of His Last Days**
by Mark Edmundson. Bloomsbury USA, 2008 ($25.95)
Traces Freud's escape from Vienna, the final two years of his life, and his ideas on the rise of fascism and fundamentalism.

FROM EDOUARD DE MONTULÉ, *TRAVELS IN AMERICA*, 1821 (*mastodon*); DPA/CORBIS (*Einstein*)

Q How does *food's appearance or smell* influence the way it tastes?

Dana M. Small, a neuroscientist at the John B. Pierce Laboratory and the Yale School of Medicine, replies:

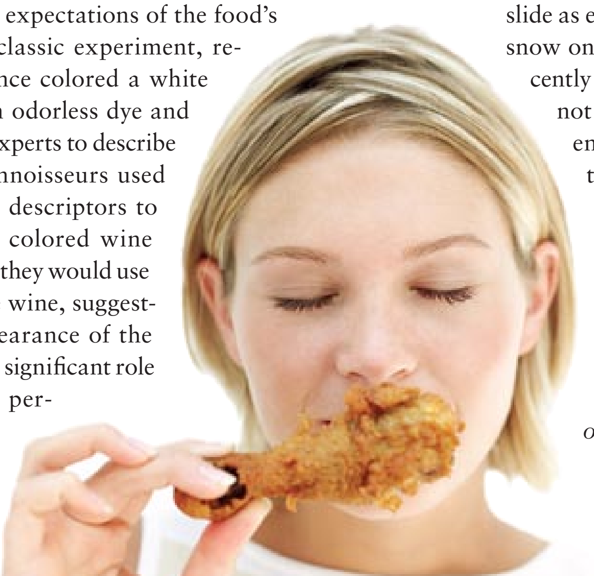
What the brain perceives as flavor is actually a fusion of a food's taste, touch and smell into a single sensation—each not only influences flavor but is an integral part of it. Sight, though not technically part of this equation, certainly influences perception in its own way.

The flavor we sense from food or drink depends partly on which taste buds it activates: sweet, sour, salty, bitter, savory or, debatably, fat. Sensory cells, located side by side with the taste buds, allow us to perceive qualities such as temperature, spiciness and creaminess. Smells also seem to come from the mouth, even though there are no cells there responsible for detecting scents. Instead the sensation depends on activation of cells located at the end of the nasal passage. The information gathered by these cells is relayed to the mouth via a process called olfactory referral.

Acquiring information related to scent through the back of the mouth is called retronasal olfaction—via the nostrils it is called orthonasal olfaction. Both methods influence flavor; aromas such as vanilla, for example, can cause something perceived as sweet to taste sweeter.

To demonstrate the phenomenon of olfactory referral for yourself, hold your nose and chew on a strawberry jelly bean. You should detect sweetness and a little sourness, along with the hard (and then soft) feeling of the candy, but you will not detect the strawberry flavor. When you let go of your nose, though, the odor-bearing molecules can travel through the nasal cavity to the smell cells, and suddenly the flavor of the jelly bean reveals itself.

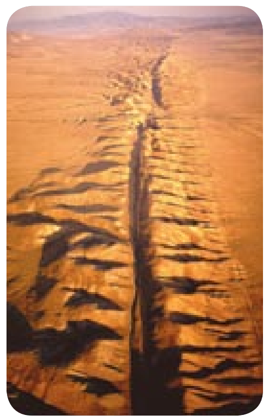
Although sight plays a less direct role than smell in the perception of flavor, it is the sense most often used to identify food, and it thereby affects expectations of the food's attributes. In a classic experiment, researchers in France colored a white wine red with an odorless dye and asked a panel of experts to describe its taste. The connoisseurs used typical red wine descriptors to characterize the colored wine rather than terms they would use to evaluate white wine, suggesting that the appearance of the beverage played a significant role in the way they perceived its flavor.



Q How do *earthquakes* come to a halt?

David D. Oglesby, a geophysicist at the University of California, Riverside, offers a response:

Simply put, an earthquake comes to a stop when the pent-up energy propelling the temblor can no longer overcome the friction holding it back.



To understand this braking process, it is important to comprehend first what makes an earthquake go. Rocks clustered around a fault—a fracture separating two blocks of rock—are held in place by friction. As time goes by, the movement of continent-size blocks of the earth's outer shell, known as tectonic plates, causes the rocks along the fault to bend and stretch, infusing them with energy like compressed springs.

When this pent-up force exceeds the friction holding the rocks, a crack on the fault forms and grows, and the fault begins to slip. This slippage releases part of the rocks' built-up energy, radiating seismic waves that travel to the earth's surface, where they can cause considerable damage.

Once the earthquake runs out of energy or encounters a sufficiently large increase in friction, it will stop. A quake can be halted in its tracks, for instance, if it hits material that does not slide as easily—that has more friction—like a skier gliding from snow onto dirt. Reaching a site where another earthquake recently occurred can also stop a temblor, because such areas do not have enough built-up energy. Or a fault might simply end; the amount of energy needed to cut a new fault through intact rock is far greater than that required to break an existing fault.

But earthquakes can also jump from one fault to another, often from as far as four kilometers away. So just as you never know when a big one will hit, it is hard to say when—or where—it might stop. ■

HAVE A QUESTION?... *Send it to experts@SciAm.com or go to* **www.SciAm.com/asktheexperts**

STOCKBYTE/GETTY IMAGES (*tasting chicken*); JAMES BALOG *Getty Images* (*San Andreas fault*)