SMARTER SEARCH ENGINES • QUANTUM CLOUDS AND ATOM CHIPS

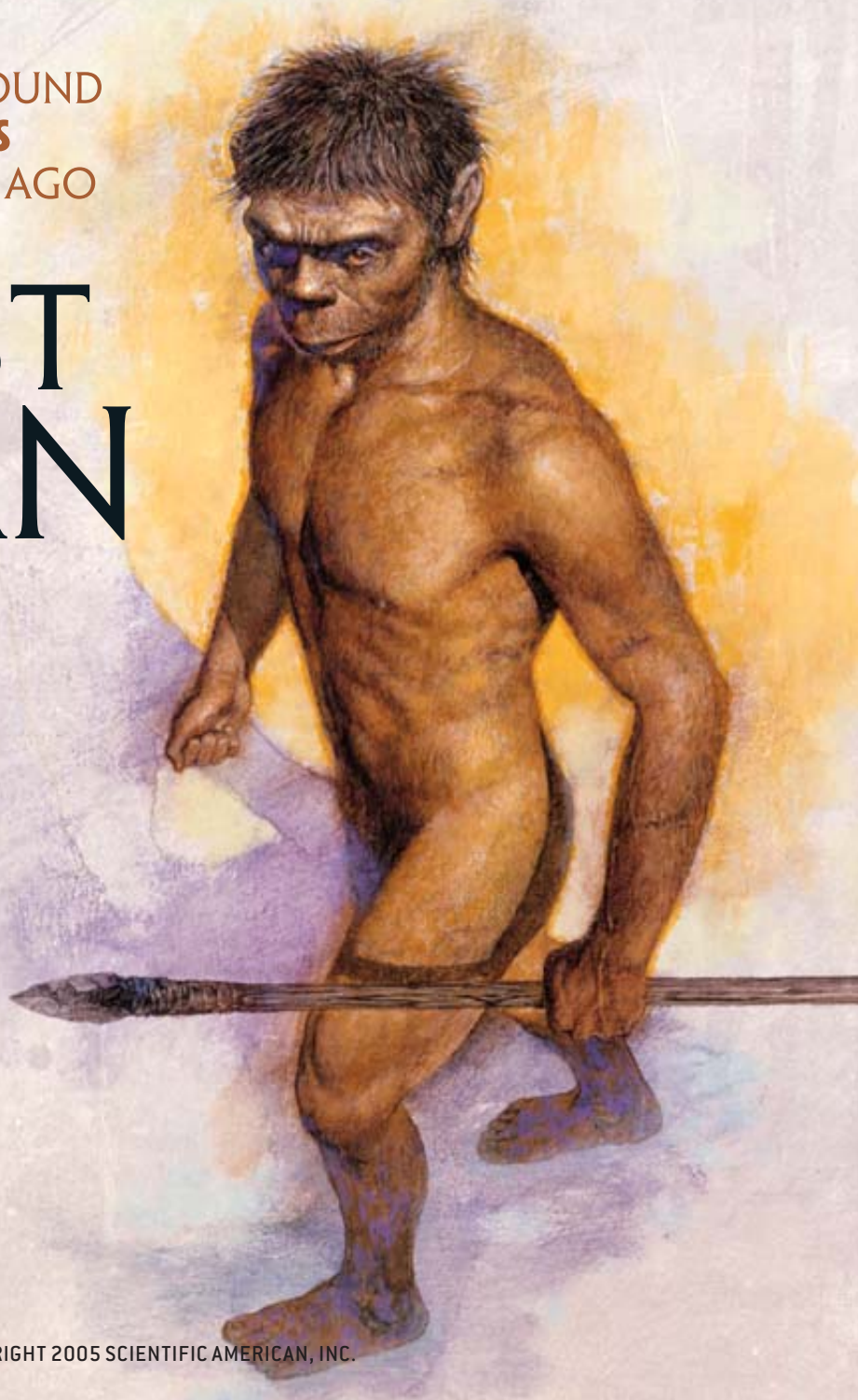
# SCIENTIFIC AMERICAN

The Year's Best **INVENTIONS** by U.S. Students

FEBRUARY 2005
WWW.SCIAM.COM

GIANT QUESTIONS SURROUND
**A CHILD-SIZE SPECIES**
FROM JUST 13,000 YEARS AGO

## THE LITTLEST HUMAN



**How Ulcer Germs Can Be Good for You**

**Nanotube Fabric for Microelectronics**

**Hardwiring Memories into Your Brain**

february 2005

# contents

## features

SCIENTIFIC AMERICAN Volume 292 Number 2


BIOTECHNOLOGY

**38 An Endangered Species in the Stomach** BY MARTIN J. BLASER

The ulcer-causing bacterium that lives in the human stomach is heading for extinction. But public health may still pay a price for that success.

APPLIED PHYSICS

**46 Atom Chips** BY JAKOB REICHEL

The coldest objects in the universe, called Bose-Einstein condensates, can be created next to the surface of room-temperature microchips. Their weird quantum behavior could be a boon to technology.

PALEOANTHROPOLOGY

**56 The Littlest Human** BY KATE WONG

Spectacular but controversial discoveries on an Indonesian island reveal that 13,000 years ago we shared the planet with a hobbit-size race of people.

INFORMATION SCIENCE

**66 Seeking Better Web Searches** BY JAVED MOSTAFA

Frustrated by deluges of not-quite-right responses from Google? New online search engines will find answers with your needs in mind.

NEUROSCIENCE

**74 Making Memories Stick** BY R. DOUGLAS FIELDS

Some memories persist while others just evaporate. The processes that help recollections last may be linked to those that shape our brains.

INNOVATION

**82 Nanotubes in the Clean Room** BY GARY STIX

Carbon nanotubes, the sooty talismans of a thousand research projects, may soon find their way into a new type of electronic memory.

TECHNOLOGY

**86 The New College Try** BY STEVE MIRSKY

The annual Collegiate Inventors Competition proves that technological creativity is alive and well on university campuses.


56 Tiny elephants and tinier people

# departments


**8 SA Perspectives**
Copyright becomes "no right to copy."

**9 How to Contact Us**

**9 On the Web**

**10 Letters**

**14 50, 100 & 150 Years Ago**

**16 News Scan**
- The Vioxx fiasco challenges drug regulation.
- The furry beast that ate dinosaurs.
- Climate changes and Amazon damage.
- Hollywood takes science to the ocean floor.
- Cosmic strings loop back.
- Terabyte storage on an optical disk.
- By the Numbers: Arctic warming.
- Data Points: Kid stuff.



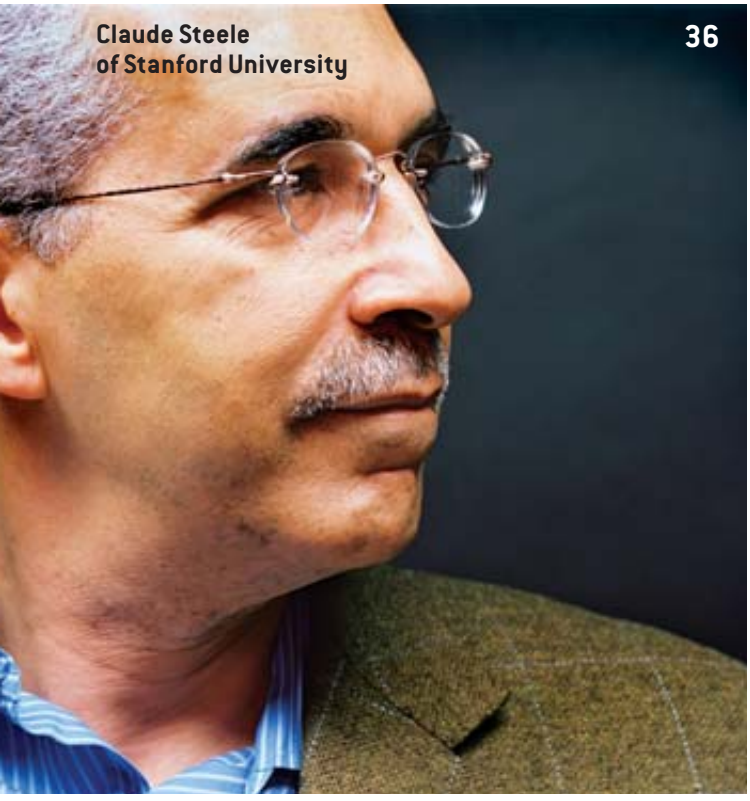


**36 Insights**
Psychologist Claude Steele's work suggests that fear of negative stereotypes hurts performance.

**92 Working Knowledge**
How new headphones cancel out unwanted background noise.

**94 Technicalities**
Dress for distress: the LifeShirt monitors vital signs.

**98 Reviews**
*Big Bang* recounts how one scientific theory for the creation of the cosmos triumphed over its competitors.


# columns


**34 Skeptic** BY MICHAEL SHERMER
The author's alien abduction experience.

**104 Anti Gravity** BY STEVE MIRSKY
Warning: Real science may shock you.

**106 Ask the Experts**
Why do bags form under the eyes?
Who determines the abbreviations for the elements?


**Cover painting by Kazuhiko Sano; photograph at left by Timothy Archibald.**

Scientific American (ISSN 0036-8733), published monthly by Scientific American, Inc., 415 Madison Avenue, New York, N.Y. 10017-1111.  Periodicals postage paid at New York, N.Y., and at additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; QST No. Q1015332537. Publication Mail Agreement #40012504. Return undeliverable mail to Scientific American, P.O. Box 819, Stn Main, Markham, ON L3P 8A2. Subscription rates: one year $34.97, Canada $49 USD, International $55 USD. Postmaster: Send address changes to Scientific American, Box 3187, Harlan, Iowa 51537. **Reprints available:** write Reprint Department, Scientific American, Inc., 415 Madison Avenue, New York, N.Y. 10017-1111; (212) 451-8877; fax: (212) 355-0408 or send e-mail to sacust@sciam.com **Subscription inquiries: U.S. and Canada (800) 333-1199; other (515) 247-7631.** Printed in U.S.A.

# Beyond the Big ©

**If William Shakespeare were working today** on Broadway or in London's West End, he would be spending a lot of time with lawyers. The Bard adapted *Romeo and Juliet* from Arthur Brooke's poem *The Tragicall Historye of Romeus and Juliet,* which Brooke, in his turn, had based on a French translation by Pierre Boaistuau of various Italian stories.

The history of creative works, whether *Romeo and Juliet* or the Beastie Boys' "Pass the Mic," is a chronicle of "borrowing" from others. Intellectual-property lawyers might use a harsher word. But the framers of the Constitution always intended to provide owners of creative works with only limited monopolies, ensuring that the public gets the right to fashion new works from old.


Over the years, however, Congress, sometimes at the behest of media companies, has erected immense barriers to derivative works by extending repeatedly both the length and the scope of copyright protection. A copyright holder no longer has to register a new work. Any blog, poet's sonnet or even a child's crayoned drawing now receives copyright automatically. Permission is needed for republishing or excerpting, with limited exemptions for fair use.

Copyright in its current form fails to strike a balance between the extremes of allowing total control over every work—"all rights reserved"—and an anarchic system in which pirates steal wantonly without recompense to owners. Overly strong property rights can threaten the Internet as a medium capable of fostering dynamic interchange of ideas.

In 2001 Stanford University legal scholar Lawrence Lessig set about righting this imbalance by becoming the leading force behind Creative Commons, a nonprofit group that furnishes a much needed middle ground that lets owners give up some but not all of their rights. An author still retains a copyright, but only some rights are reserved by choosing among the dozen or so free licenses, denoted by the Creative Commons's ⓒ mark, that are available for downloading off the Web. One license permits others to use a work as long as attribution is given. Another gives the right to sample (take a snippet to mix with music or other content) as long as the entire work is not used.

Some five million Creative Commons licenses are in use. The BBC plans to license archival material to the British public without a fee as long as it is not used for commercial purposes. The Massachusetts Institute of Technology exploits the licenses to give free access to excellent online course materials. Creative Commons has started a Science Commons effort that will even explore the open licensing of technology contained in some patents. The Public Library of Science already takes advantage of one of the licenses to specify the conditions under which scientific journal articles are made available free of charge.

The Internet, as a universal publisher of sorts, needs to be more than an outlet for commercial interests. Nascent communities of artists, scientists and nonprofits want some way to share and rework one another's intellectual output without the enormous legal burdens that come with increasingly draconian rights management. The entertainment industry has been largely silent on this issue—its idea of innovation having been the launching of lawsuits against 10-year-olds to punish music pirating. In this environment, the introduction of Creative Commons's middle path of "some rights reserved" is surely a welcome arrival.

**THE EDITORS** editors@sciam.com

JOHNNY JOHNSON

# How to Contact Us

### EDITORIAL

**For Letters to the Editors:**
Letters to the Editors
Scientific American
415 Madison Ave.
New York, NY 10017-1111
*or*
editors@sciam.com
Please include your name and mailing address, and cite the article and the issue in which it appeared. Letters may be edited for length and clarity. We regret that we cannot answer all correspondence.

**For general inquiries:**
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-754-0550
fax: 212-755-1976
*or*
editors@sciam.com

### SUBSCRIPTIONS

**For new subscriptions, renewals, gifts, payments, and changes of address:**
U.S. and Canada
800-333-1199
Outside North America
515-247-7631
*or*
www.sciam.com
*or*
Scientific American
Box 3187
Harlan, IA 51537

### REPRINTS

**To order reprints of articles:**
Reprint Department
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-451-8877
fax: 212-355-0408
reprints@sciam.com

### PERMISSIONS

**For permission to copy or reuse material from *SA*:**
www.sciam.com/permissions
*or*
212-451-8546 for procedures
*or*
Permissions Department
Scientific American
415 Madison Ave.
New York, NY 10017-1111
Please allow three to six weeks for processing.

### ADVERTISING

www.sciam.com has electronic contact information for sales representatives of Scientific American in all regions of the U.S. and in other countries.

**New York**
Scientific American
415 Madison Ave.
New York, NY 10017-1111
212-451-8893
fax: 212-754-1138

**Los Angeles**
310-234-2699
fax: 310-234-2670

**San Francisco**
415-403-9030
fax: 415-403-9033

**Detroit**
Karen Teegarden & Associates
248-642-1773
fax: 248-642-6138

**Midwest**
Derr Media Group
847-615-1921
fax: 847-735-1457

**Southeast**
Publicitas North America, Inc.
404-262-9218
fax: 404-262-3746

**Southwest**
Publicitas North America, Inc.
972-386-6186
fax: 972-233-9819

**Direct Response**
Special Aditions
914-461-3269
fax: 914-461-3433

**Belgium**
Publicitas Media S.A.
+32-(0)2-639-8420
fax: +32-(0)2-639-8430

**Canada**
Derr Media Group
847-615-1921
fax: 847-735-1457

**France and Switzerland**
PEM-PEMA
+33-1-46-37-2117
fax: +33-1-47-38-6329

**Germany**
Publicitas Germany GmbH
+49-211-862-092-0
fax: +49-211-862-092-21

**Hong Kong**
Hutton Media Limited
+852-2528-9135
fax: +852-2528-9281

**India**
Convergence Media
+91-22-2414-4808
fax: +91-22-2414-5594

**Japan**
Pacific Business, Inc.
+813-3661-6138
fax: +813-3661-6139

**Korea**
Biscom, Inc.
+822-739-7840
fax: +822-732-3662

**Middle East**
Peter Smith Media & Marketing
+44-140-484-1321
fax: +44-140-484-1320

**Scandinavia and Finland**
Publicitas Nordic AB
+46-8-442-7050
fax: +46-8-442-7059

**U.K.**
The Powers Turner Group
+44-207-592-8331
fax: +44-207-630-9922

# On the Web

WWW.SCIAM.COM

## UPDATED EVERY WEEKDAY

**Visit www.sciam.com/ontheweb to find these recent additions to the site:**

### Sleep Deprivation Tied to Shifts in Hunger Hormones

**Not getting enough shut-eye** could be interfering with your ability to shed unwanted pounds. Previous studies have shown that sleep may be a key regulator of body weight and metabolism. Now researchers have linked changes in two important appetite-regulating hormones to the amount of sleep people regularly get.

### Study Paints Our Sun as a Planet Thief

**A close encounter** between our sun and a passing star some four billion years ago may have played a role in shaping our solar system. New computer simulations describe how a rendezvous between two young solar systems could have occurred. And one potential scenario shows our sun kidnapping a planet or smaller object from the other star's entourage.

### New channels on Scientific American.com

**Health**
The latest medical breakthroughs and advice for healthy living.

**Environment**
Authoritative reporting on the state of the planet and its inhabitants.

### EXCLUSIVE ONLINE ISSUE

**Extreme Engineering**
From nanotechnology to bridge building, this issue celebrates some of the most extraordinary engineering feats of our time.

Purchase today for $5 at Scientific American Digital
**www.sciamdigital.com**

UNIVERSITY OF UTAH/SMITHSONIAN ASTROPHYSICAL OBSERVATORY

SCIENTIFIC AMERICAN®
Established 1845



# Letters

EDITORS@SCIAM.COM

**THE COVER STORY for October 2004, "Controlling Hurricanes," could not have been more timely, coming out as Florida suffered devastating visits from four major hurricanes.**

**Many readers drew hope from the possibility of either dissipating or diverting these storms. Others offered a slew of their own ideas on how to accomplish such a feat, whose success could be considered a step toward the ultimate accomplishment in humanity's age-old drive to tame the environment—controlling the weather. Yet many other readers expressed concern about the consequences. David Laden of Virginia Beach, Va., writes, "The rainfall from hurricanes can break droughts." Whereas Richard Foy of Redondo Beach, Calif., writes, "It is fascinating that you leave out the most effective way of controlling hurricanes—reducing global warming." Robert H. Myers of South Russell, Ohio, poses the question: "Are we truly so arrogant and stupid to think that altering these storms is a good thing? Once again, the technology of 'what we can do' has far outstripped the ethical concept of 'should we?'"**

**A storm of controversy as well as calm assessments on this and other topics follows.**


## CLEAN AIR VS. CLEAR SKIES

**Your SA Perspectives** editorial "Breathing Difficulties" fell flat in its description of clean air law. You claim that the Bush administration has rewritten new source review (NSR) rules that restrict the EPA's ability to compel older power plants to install pollution controls.

Yet new source review was put into the Clean Air Act to clean up new sources, not old—hence the name. It was meant to apply only to old sources if they were modified so substantially that they, in essence, became new.

Rather than distorting the law into something it is not, President Bush proposed legislation to reduce power plant emissions of sulfur dioxide and other pollutants by 70 percent, and I sponsored that legislation in the Senate. Most of the reductions would come from older, dirtier plants. Furthermore, even distorting the NSR to apply to older plants could not achieve the pollution cuts as much as would the administration's bill.

**Senator James M. Inhofe**
Chairman, Committee on Environment and Public Works, U.S. Senate

*THE EDITORS REPLY: The 1977 amendment to the Clean Air Act specifically calls for cleaning up older power plants receiving anything more than maintenance changes. The Bush administration, however, has redefined "maintenance" as any change costing up to 20 percent of a plant's worth. By this reasoning, in five years a plant could be completely replaced without ever qualifying as a new source. Does Senator Inhofe really believe that was the intention of Congress?*

*The proposed Clear Skies Initiative would cut emissions, but not as much as if the EPA now enforced all the provisions of the Clean Air Act. For instance, Clear Skies would restrict annual total sulfur dioxide emissions to three million tons by 2018, but Clean Air could cap them at two million tons by 2012.*

## STORMY WEATHER

**I found** "Controlling Hurricanes," by Ross N. Hoffman, most interesting. But having seen the results of human modification of places such as the Everglades, I am a bit dubious of the "modification" of natural phenomena on the scale of hurricanes.

When I studied meteorology, I was taught that hurricanes were a vital part of the system that transfers energy from the tropics to the middle and upper latitudes. I wonder if the researchers had considered in their simulations how messing around with hurricanes would affect this delicate balance?

The real solution is to build structures able to withstand a class 5 or high-

er hurricane or not to allow people to build in areas that are subject to natural calamities while expecting the taxpayers or insurance companies to help them rebuild after every devastating storm.

**Harold A. Climer**
Department of Physics, Geology and Astronomy
University of Tennessee at Chattanooga

## NEW LOOK AT ANCIENT GENES

**After reading** the article by John S. Mattick—"The Hidden Genetic Program of Complex Organisms"—I have come to believe the attitude toward noncoding sequences in the human genome must change. Although it might take much effort and time to decipher rules governing RNA shape and function, the fact that at least some noncoding regions are preserved during evolution might help. These regions should be checked in persons who have an increased risk of some types of cancer or other chronic diseases of uncertain etiology. It is possible that some genetically unexplained diseases result from a combination of defective genes and defective noncoding genomic regions.

**Sven Kurbel**
Osijek Clinical Hospital
Croatia

## BETTER VOTING?

**In his article** "Fixing the Vote," Ted Selker discusses the danger of fraud in touch-screen voting machines. The problem is that the voter has no way of knowing whether his or her choices shown on the screen are the ones the machine registers. The remedy urged by most computer scientists is a printout, which, after verification by the voter, drops visibly into a ballot box.

Selker criticizes this and offers as a "better option" an auditory verification heard through earphones. But this suffers from exactly the same defect as the touch screen: How do you know that the message you hear is the same one recorded on tape? Answer: you don't.

**Frank W. Sinden**
Princeton, N.J.

***SELKER REPLIES:*** *The illustration of the audio-verification scheme fell just short of showing an ideal version of that system. The earphone wires should come from the tape recorder, which should be visible to the voter. That arrangement allows the voter to visually verify that the audio he or she hears is the same as that recorded on the tape. The off-the-shelf nature of the recording device eliminates the possibility of a fraudulent voting record.*

ELECTRONIC VOTING MACHINE—Diebold Election Systems's AccuVote TSX—was decertified in California.

## CLARIFYING TRANSPARENCY

**I imagine it isn't often** that the very first sentence of a *Scientific American* article contains a factual error. Nevertheless, it occurs in "Dying to See," by Ralf Dahm, who writes, "The lens of the eye is the only transparent tissue in the human body." Isn't the cornea, the tissue through which light must *first* pass before it enters the lens, also transparent?

**Greg Martin**
via e-mail

***DAHM REPLIES:*** *It is correct to say that the cornea is transparent (as I pointed out later in the article). Yet with a thickness of only about half a millimeter, the cornea is considerably thinner than a lens. Most important, the transparency of the cornea is not cellular, as in the lens. The cornea comprises only about five layers of epithelial cells, including the outer surface, a monolayer of cells inside and a few scattered fibroblasts between these two. This compares with the 1,000 or so cell layers in a lens. As a consequence, cornea cells do not have to develop any of the radical specializations found in lens fiber cells.*

*Nevertheless, the cornea's transparency is not trivial. The bulk of the cornea is made up of collagen fibers, with complex sugar molecules filling the spaces in between. The fibers have a very regular diameter and are precisely aligned to minimize light scatter. Moreover, the amount of water in the cornea is tightly controlled to ensure its transparency.*

## FAITH-BASED GENES

**Carl Zimmer's analysis** of *The God Gene*, by Dean Hamer [Reviews], was refreshingly commonsensical and humorous, just as the book deserves. Science often suffers in journalism, with radical scientists' ideas getting most of the attention. Between the skeptics' view that all theories that challenge established science must be rejected and the tendency of others to rush to press with preliminary results, it is easy to lose sight of the largely unrecognized diligent work of ordinary scientists. The search for knowledge usually does not lead to fame.

**Lisa Michels**
Vancouver, Wash.

**ERRATA** In Francis Crick's obituary on page 41, the title of his and Christof Koch's September 1992 *Scientific American* article was incorrectly identified. The actual title is "The Problem of Consciousness."

In "The Myth Is the Message," by Michael Shermer [Skeptic], the distance from Athens to the ruins of Helice, Greece, was given as 40 miles. They are about 100 miles apart.

In an unfortunate oversight, India was excluded from the world map in "Energy Geopolitics," by Rodger Doyle [By the Numbers]. With natural gas reserves of 30.1 trillion cubic feet, or 0.5 percent of the world total, it would have been an unhighlighted country.

In the "Brief Points" about cinnamon oil's ability to kill mosquito larvae, the nonlethal insect repellent DEET was incorrectly identified as an insecticide.

# 150, 100 & 50 Years Ago

FROM *SCIENTIFIC AMERICAN*

## Eloquent Bubbles ▪ Radioactive Earth ▪ Geological Clock

### FEBRUARY 1955

BUBBLE CHAMBER—"In their exploration of the submicroscopic world of atomic nuclei, physicists are like men groping in a dark cave with a flashlight. It would help if they had a better flashlight. Physical chemists have long known that in a clean, smooth-walled vessel a very pure liquid may be heated above its usual boiling point without boiling. I wondered whether a flying particle might, under suitable conditions, trigger the formation of the microscopic bubbles that start the boiling process. If so, it might make a visible track in superheated liquid.—Donald A. Glaser" [*Editors' note: Glaser won the 1960 Nobel Prize in Physics for the invention of the bubble chamber.*]

FLUORIDATION FIGHT—"Many people, particularly scientists, believe that we are suffering in the U.S. from a national epidemic of irrationality—what Senator J. W. Fulbright of Arkansas has called the 'swinish blight of anti-intellectualism.' Fluoridation of public water supplies has been recommended by an impressive list of scientific organizations. However, from the beginning there has been opposition. The anti-fluoridation argument has three main themes: 1. fluoridation is an experiment which has not proved its value and may hold unknown dangers; 2. fluorides are poisons; 3. treatment by public agencies of the water that everyone must drink is a step in the direction of socialized medicine and an invasion of individual rights."

### FEBRUARY 1905

OUR HOT EARTH—"Prof. Rutherford notes that 'While the heat supplied by possible chemical combination is quite inadequate to account for the heat of the sun and earth, the recent discovery that the radioactive bodies are able to emit an amount of heat about one million times greater than is evolved in the most violent chemical reaction, has thrown quite another light on the question. The calculations of the age of the earth made by Lord Kelvin, which were based on the theory that the earth was a simple cooling body in which there was no further generation of heat, cannot apply, for the present temperature gradient of the earth may have been nearly the same for a long interval of time.'"

A JUMBO DELAY—"A circus train was pulling out of Spokane, Wash., a few weeks ago, when suddenly the engine 'broke.' The water tank was found to be nearly empty, although filled at the water crane but a short time before. No explanation of this mystifying condition was apparent until water was seen running from the elephant car next to the tender. Apparently 'Jumbo' had amused himself by reaching his trunk through the open end of his car into the manhole of the tender and sucking up the water, with which he had deluged the other animals in the car. They looked like 'drowned rats,' and needless to say had enjoyed their involuntary baths no more than the trainman had the delay."


CLEANER WINDOWS through invention, 1855

### FEBRUARY 1855

EARTH AGE AND FAITH—"A question of great importance at the present day is that of the age of our planet, and the changes which have taken place upon it, as related in Genesis. One class believe that the successive acts of creation mentioned in Genesis took place in the exact order there described, but that instead of the days there mentioned being solar days, they were *indefinite periods of time*—some of them of great length—perhaps sixty thousand years. This latter class embrace the greatest number of learned geologists and divines. Sir Charles Lyell believes that it must have taken 67,000 years to form the delta of the Mississippi."

WINDOW WASHER—"The annexed figure is a perspective view of a patented method and apparatus for washing windows. The improvement enables any person to wash windows by ejecting a stream of water upon them from the nozzle of a pipe, and by employing no other means to do so, than a pail, a post, and tube."

POLICY

# Avoiding Another Vioxx

GUARDING AGAINST UNSAFE DRUGS MEANS MAJOR CHANGES **BY SARA BEARDSLEY**

**"Too cozy"** is how Senator Charles Grassley of Iowa referred to the relationship between the U.S. Food and Drug Administration and pharmaceutical companies in the aftermath of the Vioxx debacle. Although the FDA admits no substantive lapse in vigilance, congressional pressure and consumer outrage are forcing officials to rethink the agency's role and perhaps even the drug approval process itself.

The furor began last September, when Merck, Vioxx's manufacturer, withdrew the popular anti-inflammatory drug after a study revealed that long-term use doubled the risk of heart attack and stroke. In a congressional hearing last November, David J. Graham, a drug safety reviewer at the agency, estimated that as many as 55,000 Americans may have died as a result of taking the painkiller, a member of the COX-2 inhibitor class of drugs.

EMBATTLED: Merck CEO Raymond Gilmartin, whose company made the painkiller Vioxx, looks on as David J. Graham, associate director for science at the FDA's Office of Drug Safety, spells out the oversight errors culminating in the drug's withdrawal in a Senate hearing last November.

KEVIN LAMARQUE/REUTERS/CORBIS

Worse, early studies had shown elevated cardiovascular risks for patients taking Vioxx, but the FDA took no action against the drug other than adding a "precaution" to its label in 2002. Such a response led Graham to testify that "the FDA, as currently configured, is incapable of protecting America against another Vioxx."

FDA officials have defended themselves by claiming that they lacked enough information to order a recall of Vioxx. Sandra Kweder, deputy director of the FDA's office of new drugs, says the agency and its advisory committee were "stumped" by the conflicting results of studies done before and after Vioxx was approved in 1999.

Medical experts point out, however, that this confusion arises from the systemic problems surrounding unreliable preapproval trials and an inadequate system for monitoring new drugs after they come on the market. Because many adverse drug effects are rare or hard to detect, researchers often cannot grasp the full extent of the dangers until hundreds of thousands of patients are taking the medication. (The clinical trials required for FDA approval typi-

cally involve no more than a few thousand subjects and can, as in the case of Vioxx, be too short-lived to indicate long-term trends.) The FDA orders drug companies to conduct postmarketing research as a condition of approval, but fewer than half of such studies are actually completed. And the FDA's MedWatch program, which gathers reports of adverse effects voluntarily submitted by doctors, has garnered criticism from prominent medical journals and epidemiologists for its underreporting and unreliability.

The current problems appear to stem in part from the 1992 Prescription Drug User Fee Act, which sought to speed the introduction of new drugs by allowing the FDA to accept user fees from pharmaceutical companies, which were then siphoned into hiring additional drug reviewers. By focusing the agency's resources on the approval process, the law left less money for postapproval monitoring. Drummond Rennie, a deputy editor of the *Journal of the American Medical Association,* says the financial contributions of the drug companies have also made the FDA less likely to confront them. "The FDA has lost its will and courage," he asserts.

To remedy the situation, Senator Grassley has proposed an independent body for oversight. "It doesn't make sense from an accountability standpoint to have the office that reviews the safety of drugs already on the market to be under the thumb of the office that puts drugs on the market in the first place," he contends. Other policymakers have urged the FDA to be more aggressive about adding warnings to drug labels or to establish a public database containing the results of all major drug studies so that consumers can make more informed decisions. Under scrutiny, the FDA has hired the National Academy of Sciences's Institute of Medicine to study possible changes to the drug safety system.

The Vioxx withdrawal may also mark a turning point for the industry. Instead of seeking blockbuster drugs aimed at large numbers of consumers, companies may focus on niche medications designed for particular groups of ailing people. Garret A. FitzGerald of the University of Pennsylvania School of Medicine, an expert on COX-2 inhibitors, notes that Vioxx might have been able to stay on the market if its use had been restricted to people who have a low risk of cardiovascular disease but a history of gastrointestinal problems. (Vioxx is less likely to irritate the digestive tract than nonprescription painkillers.) "Here are drugs that are very useful in a segmented market," he says, "and their usefulness is being put at risk by the pursuit of a blockbuster strategy. I think, inevitably, the trend is going to be toward more segmented indications."

### THREATS FROM VIOXX'S COUSINS

**Like Vioxx, Celebrex and Bextra work by inhibiting the function of cyclooxygenase-2 (COX-2), an enzyme that produces the prostaglandins that cause inflammation. One of these molecules, prostaglandin $I_2$, appears to prevent damage to artery walls and the clumping of blood platelets; because all the COX-2 inhibitors curtail its production, researchers feared that Celebrex and Bextra may also raise cardiovascular risks.**

**That fear has come true: last December, Pfizer announced that in one trial moderate doses of Celebrex produced cardiovascular risks comparable to those of Vioxx, doubling the rate of heart attack and stroke. The company also warned doctors in late 2004 about Bextra's adverse effects on cardiac surgery patients. The FDA plans to review studies of the COX-2 inhibitors at an advisory committee meeting this month.**

PALEONTOLOGY

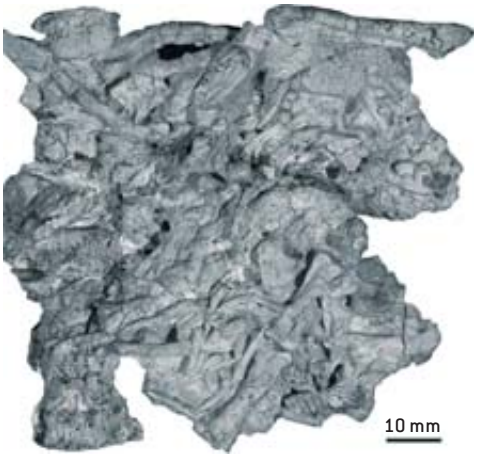
# Hungry for Dino Meat

## A POINTY-TOOTHED MAMMAL THAT PREYED ON DINOSAURS

BY CHARLES Q. CHOI

**Early mammals conjure up** images of rat- or shrew-size creatures that skulked in the shadows of dinosaurs, trying to avoid being ripped limb from limb by the terrible lizards. Now it seems that the hunted sometimes became the hunter. Newfound fossils reveal a baby dinosaur inside a mammal's gut—the first direct evidence of such predation.

An international team based its conclusions on a species called *Repenomamus robustus,* a mammal about as big as a Virginia opossum that lived during the Mesozoic, 130 million or so years ago. Within the rib cage of *R. robustus* was the skeleton of a young dinosaur whose serrated teeth, limbs and toes mark it as *Psittacosaurus,* a hornless relative of *Triceratops* that reached cow proportions in adulthood. Whereas the mammal's bones are preserved in their anatomical position, the dinosaur's are mostly fragmented and packed together where the stomach lies in living mammals. "The most likely explanation is that it was eaten," concludes Jin


CRETACEOUS KILLER? Mammals of the *Repenomamus* species (*R. giganticus, top*) may have hunted dinosaurs. The fossil of a young dinosaur (*bottom*) was found compacted inside the stomach area of *R. robustus*.

Meng, a paleontologist at the American Museum of Natural History in New York City. The findings were scheduled to have appeared in the January 13 issue of *Nature*.

Fossils with stomach contents are rare. Dinosaurs with mammal jaws in their guts had been discovered earlier. "This is the opposite case," Meng says of *R. robustus*.

Other members of *Repenomamus* also seemed capable of dining on dinosaurs. Among the other dog-size, shrewlike species dug up by local farmers in the Yixian formation of northeast China, where caches of fossilized feathered dinosaurs are common, researchers discovered *R. giganticus*. About as big as a Tasmanian devil, this creature was the biggest of its genus, reaching 12 to 14 kilograms in weight and growing to more than a meter in length. Its skull was 16 centimeters long, 50 percent larger than that of *R. robustus*, the next largest species. "Big implies many things. They need more food and a larger home range to walk around in, and they have the capability to eat larger prey and resist predation from carnivorous dinosaurs," Meng explains. "They might also live longer and move faster."

The new fossils were found buried in sandstone flecked with volcanic ash. Fossils discovered in layers above the mammals' bones were squashed, which suggests that they dropped into a lake and were gradually covered by mud, which compressed them flat. In contrast, the *Repenomamus* mammals were preserved three-dimensionally articulated, suggesting that they died quickly en masse by a volcanic eruption.

Although Meng's team, which includes colleagues from the Chinese Academy of Sciences in Beijing, cannot exclude the possibility that the *Repenoma* family was a clan of scavengers, Meng argues that its large, pointed teeth and jaws were good for catching, holding and rending other animals—abilities more indicative of a predator than a scavenger. Some of the dinosaur's long bones were still articulated, "meaning they were swallowed in large chunks," Meng reasons. In addition, the dinosaur's skull was roughly a third the length of the mammal's, "not just a snack" but a meal challenging enough to discourage a casual diner, he adds. Scavengers are also relatively rare among mammals: among extant carnivorous mammals, only two hyena species are habitual scavengers.

Paleontologist Zhe-Xi Luo of the Carnegie Museum of Natural History in Pittsburgh called the findings the first unambiguous proof early mammals were more than insect eaters. Paleontologist Spencer Lucas of the New Mexico Museum of Natural History and Science in Albuquerque agrees: "Dinosaurs are often thought of as dominating the Mesozoic, but this shows mammals weren't above having a Dinosaur McNugget."

*Charles Q. Choi, based in New York City, is a frequent contributor.*

## STAYING SMALL

**Mesozoic mammals remained small, scientists speculate, because dinosaurs were entrenched well enough as large carnivores and herbivores to prevent mammals from invading those niches. In this way, they kept early mammals from evolutionary experiments in large body sizes. The newly discovered *Repenomamus giganticus*, the largest mammal ever found in the dinosaur age, significantly raises the upper limit. In fact, it is actually larger than several small dinosaurs (particularly the dromaeosaurids, such as the feathered dinosaur *Microraptor*).**

***R. giganticus* probably lived in a dense, very warm and humid forest, most likely by a lake. The anatomy of its feet and hands suggests it was not good at grasping, ruling out an arboreal life. Instead it seemed better suited to life on the ground, in the shade of the Mesozoic's mossy ferns and ginkgo trees.**

FROM YAOMING HU, JIN MENG, YUANQING WANG AND CHUANKUI LI IN *NATURE*, VOL. 433, NO. 7022, JANUARY 13, 2005

ECOLOGY

# Punctuated Disequilibrium

OCCASIONAL BUT EXTREME CLIMATE COULD TURN PARTS OF THE AMAZON RAIN FOREST INTO DRY SAVANNAS **BY CLAUDIO ANGELO**

**With a bit more warmth** and extra fertilizer, a plant can go from limp to lush. But all the good things for flora are meaningless without water. According to recent analyses, large parts of the Amazon rain forest, which sprawls across an area about as large as western Europe, could end up turning into dry savannas—a state from which there may be no turning back even if the climate returned to normal.

This somber prediction comes out of the latest findings of the Large Scale Biosphere/Atmosphere Experiment in Amazonia, the most ambitious field project ever done in a tropical ecosystem. Since 1999 the experiment, sponsored by the Brazilian government, NASA and the European Union, has brought together 800 scientists, who have been probing the six-million-square-kilometer jungle with instrument-laden towers, airplanes and satellites in a quest to understand how the forest works.

The researchers still have a long way to go for a complete picture. But they think they now know enough to begin to assess how the complex Amazon ecosystem will react to global warming, increased carbon dioxide (which acts as fertilizer) and other changes. Two studies in the project suggest a trend toward the formation of savannas at the eastern and southern parts of the forest.

A key factor is deforestation, which alone in the eastern Amazon could tip the ecosystem toward a drier state. Plants in that region, which is naturally drier than other parts of the forest, help to keep moisture in the area by recycling water through evaporation and transpiration. Without the flora, drought sets in. The mean temperature also goes up.

Change in land use may also dry up the forest in a less straightforward way: by altering the physical properties of rain clouds. In a series of experiments carried out with aircraft flying through smoke plumes during forest fires, a team led by physicist Maria Assunção da Silva Dias of the National Institute for Space Research and her colleague Paulo Artaxo of the University of São Paulo has found that smoke aerosols probably inhibit formation of big water drops, producing clouds that are incapable of rain.

Climatologist Carlos A. Nobre, a

DRYING OUT: *Cerrado,* a type of savanna that dominates Brazil, may develop in parts of the Amazon rain forest because of continuing climate change and deforestation.

TUI DE ROY *Minden Pictures*

leading scientist at the Brazilian National Institute for Space Research, has factored the effects of deforestation and global warming into a computer model that couples vegetation changes with standard global circulation models. In one of Nobre's scenarios, by 2100 up to 60 percent of the forest will turn into *cerrado,* the type of savanna that dominates the landscape in central Brazil. Such a shift in land cover might be hard to reverse. "We are forcing the forest system into a new state of equilibrium," he says.

The effects of warming by itself are harder to elucidate. But atmospheric scientist Steven C. Wofsy of Harvard University and his colleagues have devised a novel way to estimate the impact of climate change on the current state of the forest. The researchers looked at the likelihood of extreme events, such as abnormal droughts, and matched them to field observations of the drought-sensitive vegetation of Tapajós National Forest in central-eastern Amazonia in the Brazilian state of Pará. They then used their model to generate a simulation spanning 2,500 years and found that forest gives way to *cerrado* when more than 33 years of drought occur in a century. "You end up bisecting the Amazon with savannas," remarks Lucy Hutyra, a member of Wofsy's team.

The take-home message, she says, is that the extremes are more important than the averages. In a global change scenario, the temperature can rise without signs of ecosystem disturbance in the Amazon. But on the scale of centuries, some areas of the forest, such as the Tapajós region, are highly sensitive to variability. "There is a lot of deadwood and fuel for fire," Wofsy explains. "Suppose you have 10 or 20 years in which nothing happens, then one of those droughts strikes and there is a fire. If the fire isn't too severe, the forest recovers. If it comes again in 25 years or 15 years, everything is destroyed."

*Claudio Angelo is science news editor of the Brazilian daily newspaper* Folha de S. Paulo.

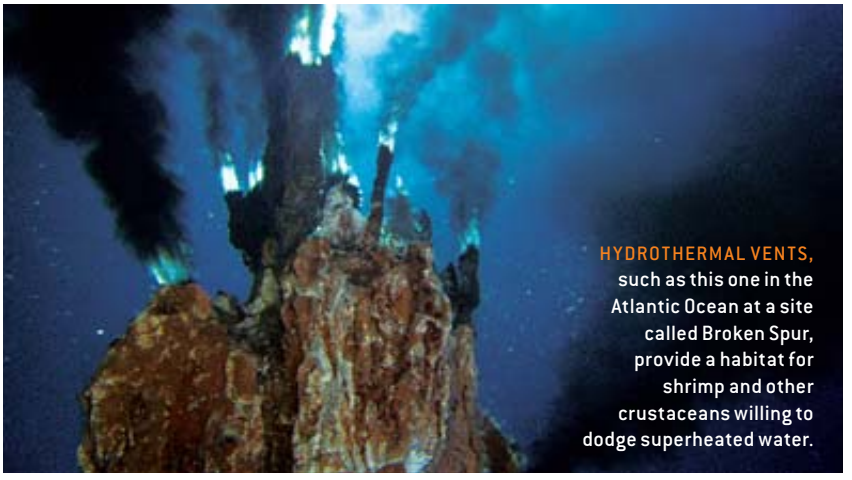
OCEANS

# Into the Abyss

SCIENCE MEETS ENTERTAINMENT AT THE BOTTOM OF THE SEA **BY CHRISTINA REED**

*"Mission Control. Mission Control. Mir 1—Beginning our descent. Over."*
*"Roger that, Mir 1."*

**The date is** August 7, 2003, and I am inside the Russian *Mir 1* submersible in the Atlantic Ocean. With me are cameraman Vince Pace and pilot Anatoly Sagalevitch, and our bodies rapidly heat up the two-meter-wide sphere to 30 degrees Celsius. Fortunately, the sub quickly cools in the 30 minutes it takes to reach our destination: the "Lost City of Atlantis," where geologic formations resemble ancient ruins.



HYDROTHERMAL VENTS, such as this one in the Atlantic Ocean at a site called Broken Spur, provide a habitat for shrimp and other crustaceans willing to dodge superheated water.

Lost City was one of 10 hydrothermal vent sites that became filming locations for James Cameron's 3-D IMAX movie *Aliens of the Deep,* released January 28. The project involved two month-long expeditions, two oceans, two ships, two Russian *Mir* submersibles capable of 6,000-meter depths, two acrylic-domed *Deep Rover* submersibles capable of 1,000-meter depths, 14 scientists (a.k.a. "the talent"), 40 dives, and a slew of crew members for both ships and the production itself.

As the science coordinator, I worked as the liaison between the production crew and the scientists. For every researcher we brought out to sea, a team of scientists waited back on shore for samples, pictures and data. In a way, this was similar to other expeditions I have worked on, both as an oceanographer and as a journalist. Only this time, the ship had been converted into a floating movie set, complete with lights, camera, sound and action.

Integrating production needs with scientific ones provided a challenging dynamic. Unlike research expeditions, where investigators have upward of a year to prepare, with the film expedition I was calling scientists in June to see if they could join us in July. Over time, the scientific agenda grew to match the production agenda. I could tell because the researchers had almost as much equipment as the production crew itself.

The National Science Foundation provided Maya Tolstoy of the Lamont-Doherty Earth Observatory with 12 ocean-bottom seismometers that were heavy enough to require a forklift to move. Dijanna Figueroa, a graduate student at the University of California at Santa Barbara, brought her adviser, Jim Childress, an assistant, and the pressure housing, computers and two-meter-tall gas canisters needed to establish a biological lab at sea. They want to understand the metabolic processes of organisms around vents. Space scientists came along, too: Pamela ("Pan") Conrad and Lonne Lane of the Jet Propulsion Laboratory in Pasadena, Calif., want to perfect instruments that can detect organic chemicals and so potentially identify alien life on other worlds. They had a chance to test them on the mysterious creatures of the deep.

The life in these extreme environments is thriving because of the geology. In *Mir 1,* we traverse the bottom until we approach a cliff's edge and find a fragile outgrowth of yellowish-white carbonate minerals: examples of hydrothermal venting on 1.5-million-year-old oceanic crust. Unlike hydrothermal vents at spreading ridges, where the seawater spews to the surface heated by a magma chamber below the crust, Lost City seeps its vent fluid because of a chemical reaction occurring between the mineral olivine in the mantle rock and the seawater.

As the first sub in the water, we pick a rendezvous site and relay our *x, y* coordinates based on acoustic signals from transponders positioned earlier on the seafloor—no

## WHEN FUN PAYS FOR SCIENCE

**As the production of James Cameron's *Aliens of the Deep* unfolded, a symbiosis between the scientists and those in the entertainment industry developed. For the Russian scientists onboard the science vessel *Keldysh,* such a relationship is now standard bread-and-butter financial planning for their ship time. Besides procuring the *Keldysh*'s submersibles for Cameron's other productions—*Titanic, Ghosts of the Abyss* and *Expedition: Bismarck*—the Russian researchers allow adventure-travel firms Space Adventures and Deep Ocean Expeditions to book tourist dives to the bottom of the sea.**

GPS down here. One by one, the other subs appear—first *Mir 2* and then *Deep Rover 1* and *2*. With their acrylic domes, the rovers look like aquariums for people.

All too quickly, five hours go by—about when our 16-volt battery dies: *"Deep Rover 2. Mir 1. Jim, we have to leave. Our 16-volt is out. Call Mission Control. Let them know we're ascending. Over."*

*"Roger that. See you at the surface."*

*Christina Reed, now back in Washington, D.C., was the science coordinator for* Aliens of the Deep.

COSMOLOGY

# String Revival

## ARE COSMIC STRINGS BEHIND UNUSUAL LENSING EFFECTS? BY GOVERT SCHILLING

**Like haute couture,** cosmology has its own fads, fashions and fallacies. Gone are the heydays of galaxy surveys and quasar discoveries; now searches for the universe's first stars and for the nature of dark energy are all the rage. But like miniskirts and bell-bottoms, some castoffs experience a resurgence. In particular, cosmic strings, which fell out of favor in the late 1990s, are making a comeback thanks to observations that may have actually detected them.

Cosmic strings are hypothetical one-dimensional defects in the fabric of spacetime. Cosmologists once thought these kinky concoctions, weighing as much as one Earth mass per meter, could have caused galaxy clusters to clump. But recent measurements of the cosmic microwave background radiation, the remnant glow of the big bang, convincingly ruled out this scenario. Cosmic strings became old-fashioned almost overnight.

A U.S.-Ukrainian team of astronomers led by Rudolph E. Schild of the Harvard-Smithsonian Center for Astrophysics now claims that the mysterious behavior of a double quasar near the Big Dipper can best be explained by an intervening loop of cosmic string. The image of the quasar is being split in two by the gravity of a massive galaxy in the line of sight. Light from image B takes longer to reach Earth than that from image A, so brightness variations in B lag 417 days behind the same fluctuations in A.

In the mid-1990s, however, the two images winked synchronously—the brightnesses of both rose and fell together several times over a year. In the August 2004 *Astronomy and Astrophysics,* Schild and his colleagues show that all possible explanations for this behavior fail, except for gravitational lensing by a small loop of cosmic string close to our own Milky Way galaxy. The moving cosmic string would have acted as an additional gravitational lens, affecting both quasar images simultaneously. "It is difficult to propose a less exotic model," they conclude.

Meanwhile a Russian-Italian team found a much stronger cosmic string candidate in the constellation Corvus: a galaxy split into two uncannily similar and completely undistorted images. A normal gravitational lens produces images with different brightnesses and shapes. Intriguingly, many other gravitational lens candidates extend across the surrounding area, as if a piece of cosmic string is stretched out in the foreground. "The more we work on it, the more we think we've found a genuine cosmic string," says team member Giuseppe Longo of Federico II University in Naples.

Britain's Astronomer Royal Martin J. Rees of the University of Cambridge warns that "extraordinary claims demand extraordinary evidence, and we certainly don't yet have this from the current observations." That may change soon. Longo and his colleagues have applied for observing time on large ground telescopes and on the Hubble Space Telescope to study their mystery object in Corvus in much more detail. "If we find a very sharp edge in the image right between the two galaxies," Longo remarks, "that would constitute definitive proof."

*Govert Schilling writes about astronomy from Amersfoort, the Netherlands.*

### COSMIC STRINGS FROM SUPERSTRINGS

**Cosmic strings are no longer needed to explain the large-scale structure of the universe. But "this is certainly not to say they don't exist," says Thomas W. B. Kibble of Imperial College London, who founded cosmic string theory in 1976. In fact, recent versions of superstring theory, which describes subatomic particles as vibrating loops of string and is the leading candidate for a physical theory of everything, strongly suggest (if not demand) the existence of cosmic strings, according to Kibble. Though not fully convinced by the evidence gathered so far, he says, "I think there's quite a serious chance that cosmic strings are around and will turn up someday."**

DATA STORAGE

# More Bits in Pits

DVD-LIKE SYSTEM COULD TAKE A RUN AT HOLOGRAPHIC STORAGE **BY JR MINKEL**

PLAYING THE BLUES: DVDs will soon hold at least three times more data by relying on blue wavelengths. Changing the shape of the pits could boost the data density an additional 40-fold.

**Next-generation DVDs,** due out at year's end, promise to store at least three times as much data as today's silvery disks, enabling them to offer enough extras to keep film buffs bleary-eyed. But researchers are already working on follow-up technology and have demonstrated an approach that could boost the capacity by 40 times more.

A conventional DVD encodes 0s and 1s in the form of pits, which are read by a red laser. The pit sizes and red wavelengths limit the capacity of the disks to at most 4.7 gigabytes per layer (about eight hours of video for a four-layer disk). For DVD's next step, consortiums of electronics and computer companies have shifted the laser to blue, shortening the wavelength and thereby permitting smaller pits—and thus more pits—to be etched on the disk. Two competing formats are in play: Blu-ray (25 gigabytes of storage per layer) and HD-DVD (15 gigabytes). With multiple layers, both formats can hold a high-definition movie (about 20 to 25 gigabytes).

But future movies will exceed today's high-definition resolution, and such formats will require about four times more capacity. "There will be a lot of consumer pull for optical products of hundreds of gigabytes by 2010," says Tom Coughlin, a data storage consultant in Atascadero, Calif. Simply shifting to shorter (ultraviolet) wavelengths is challenging, however, because the clear, protective part of current disks is opaque to that kind of light.

Peter Török and his colleagues at Imperial College London have figured out a way to squeeze in more data: have individual pits encode more than one bit. They have produced asymmetric pits that look different depending on their orientation, like a lopsided crater. Shining laser light onto the pit from different angles produces different reflections and therefore can register additional bits. Last fall Török's group reported it could distinguish the reflections from pits with simple asymmetries, and it estimates that the added information could be enough to pack a terabyte (1,000 gigabytes) onto a four-layered DVD-size disk. A single disk could hold all the episodes of all the seasons of *The Simpsons*.

So far they have only demonstrated the technique, called multiplexed optical data storage (MODS), on a few pits, but Török believes that a commercial system consisting of four-layer disks could be ready between 2010 and 2015. The hardest task would be reconfiguring the lens to focus the laser correctly onto the pits, he says. The group also figures manufacturers could construct MODS disks with conventional DVD processes at pennies a disk.

The MODS disks could pose a near-term threat to the most advanced alternative for mass-storage optical technology—holography. The technique relies on a laser to reconstruct large volumes of information by focusing on a holographic "page" encoded in a polymer. Stacking the pages can result in a capacity of hundreds to thousands of gigabytes. "Just about every major consumer electronics company in data storage today is working on holographic storage," explains Brian Lawrence, optical engineer in General Electric's global research department, which is studying one type of holographic system. Holographic drives could combine terabytes of capacity with rapid data transfers. Two companies—InPhase Technologies in Longmont, Colo., and Optware in Yokohama, Japan—plan to release the first holographic drives for professional backup storage and archiving next year.

Although MODS may have the advantage of being able to use existing technology in reading data, holographic technology could probably retrieve bits faster. And after 40 years of research, the cost and engineering challenges of holographic systems are well understood, whereas MODS lacks the body of work that would allow a good comparison, notes Wolfgang Schlichting of infotech analyst group IDC. "I would caution on getting excited too early about a new technology," he advises.

*JR Minkel is a frequent contributor.*

## FIRST COME, FIRST ADOPTED

**Unless the competition offers a clear advantage, the format that arrives first often gains an edge in attracting customers and attaining dominance. In that regard, time works against any new optical storage methods. Although the first holographic drives may arrive next year for professional use, consumer versions will probably wait until the next-generation DVD format (Blu-ray or HD-DVD) has its run, typically seven years.**

**The multiplexed optical data storage system, using DVD-like pits to encode several bits, may not appear until 2010 or later. In the meantime, magnetic hard drives could grow to terabyte capacity in just two or three years, or the Internet could become the dominant means to store and transmit data.**

PIONEER CORPORATION

# Melting at the Top

RAPIDLY WARMING ARCTIC WILL HAVE GLOBAL CONSEQUENCES **BY RODGER DOYLE**


ARCTIC SEA ICE will shrivel, according to projections of the Arctic Council. The maps show the state of September sea ice for three periods in the 21st century.

**The future impact** of global warming lies in the Arctic. There temperatures have risen almost twice as fast in recent decades as in the rest of the world. The Arctic Council, an intergovernmental organization comprising eight nations—the U.S., Canada, Iceland, Denmark, Norway, Sweden, Finland and Russia—plus several indigenous peoples' organizations, issued a sobering report last November. It estimates that by late in this century, average Arctic winter temperatures will rise roughly four to seven degrees Celsius over land and seven to 10 degrees C over oceans, leading to profound changes by the end of the century.

Although most of the sun's energy reaches the tropics, the atmosphere and oceans redistribute the equatorial energy toward the poles. Unlike the tropics, where a large proportion of the energy received at the surface goes into evaporation, more of the energy received at the Arctic surface goes into warming the atmosphere. For several complicated reasons, including greater absorption of solar radiation, the Arctic is likely to heat up more than the Antarctic.

The maps, based on the average of five climate models, project the state of Arctic sea ice in September for three periods between 2010 and 2090. According to the Arctic Council, the Greenland ice sheet, the largest mass of land-based ice in the world, will probably cross the line into irreversible melting in this century. With additional melting of other land-based ice in the next few centuries, Greenland ice melting would raise ocean levels eight meters, threatening major cities such as Mumbai, Calcutta and Manila and wiping out Florida below Miami. Smaller rises would also be disastrous: 17 million people in Bangladesh live less than one meter above sea level. Moreover, as the Arctic permafrost shrank, the carbon stored there, about 14 percent of the world's total, would reinforce the greenhouse effect. Arctic warming would devastate polar bear and seal populations and disrupt the lives of the indigenous people.

On the positive side, the Northwest Passage would open within a few decades to regular summertime shipping, and opportunities for offshore oil and gas extraction would probably increase. Indeed, up to 25 percent of the planet's remaining oil and gas is in the Arctic. Natural gas hydrates, icelike crystal solids trapped below the permafrost, theoretically contain more energy than all conventional reserves of oil, natural gas and coal combined. But the full exploitation of Arctic resources to satisfy world energy needs is unlikely to be possible for many decades to come [see By the Numbers, September and October 2004].

*Rodger Doyle can be reached at rdoyle2@adelphia.net*

## FURTHER READING

**Intergovernmental Panel on Climate Change.** IPCC Special Report on Emissions Scenarios, 2000. www.ipcc.ch

**Satellite-Observed Changes in the Arctic.** Josefino C. Comiso and Claire L. Parkinson in *Physics Today*, Vol. 57, No. 8, pages 38–44; August 2004. www.physicstoday.org/vol-57/iss-8/p38.html

**Arctic Climate Impact Assessment.** Arctic Council, 2004. www.arctic-council.org/

LUCY READING-IKKANDA, SOURCE: ARCTIC CLIMATE IMPACT ASSESSMENT, 2004

## DATA POINTS: TIME SPENT

**American kids may have become more serious about academics. Investigators from the University of Michigan Institute for Social Research surveyed 2,908 U.S. children and adolescents aged six to 17 years in 2002–2003 and compared the data with a smaller survey conducted in 1981–1982.**

**Hours spent per week:**

| | 2002–2003 | 1981–1982 |
|---|---|---|
| Sleeping | 68.2 | 62.63 |
| Attending school | 32.45 | 26.35 |
| Watching television | 14.6 | 15.73 |
| Playing games | 8.08 | 7.33 |
| Eating | 7.1 | 8.47 |
| Studying | 3.97 | 2.63 |
| Playing sports | 2.98 | 4.07 |
| Using a computer | 2.75 | 0 |
| Reading | 1.28 | 1.15 |

*SOURCE:* Changing Times of American Youth: 1981–2003, *by F. Thomas Juster, Hiromi Ono and Frank P. Stafford, University of Michigan, 2004. About 20 hours per week is unaccounted for in the 1981–1982 survey, as opposed to 45 minutes in 2002–2003.*

EXTREME LIFE

## Parched Presence

LIFE exists in the bone-dry Atacama.

**The barren, Mars-like heart** of the Atacama Desert in northern Chile seemed to presage bad news for discovering life on the Red Planet. Researchers failed to find organisms in the soil, which gets rain maybe once a decade and may be as arid as places on Mars. Now Raina Maier of the University of Arizona and her colleagues have discovered that the soil is not sterile after all. They dug every 1,000 feet for a 120-mile stretch, cleaning their hand trowels with disinfectant before each scoop. Earlier researchers shoveled down to four inches; this time investigators went eight to 12 inches deep. In the November 19, 2004, *Science,* they report that, when moistened, samples from areas devoid of plant life for at least a million years yielded bacteria, which may have survived in a state of suspended animation. The NASA Phoenix mission will attempt a similar experiment on Mars in 2008. *—Charles Q. Choi*

INFECTIOUS DISEASE

## Say It, Don't Spray It

**During the SARS outbreak** in China, a handful of "super spreaders" may have transmitted the airborne disease much better than others. Supporting this idea, a group led by Harvard University researchers measured the number of microscopic fluid droplets exhaled from 11 healthy subjects and found that just six of them breathed out 98 percent of the droplets. The researchers then had the subjects inhale nebulized saline for a few minutes. The saline treatment cut the number of droplets by 66 to 80 percent for up to six hours, probably by increasing the surface tension of the mucosal linings of the lungs and thereby preventing smaller (and more easily exhaled) droplets from forming. A saline spray could reduce the spread of airborne diseases, including SARS, tuberculosis and influenza, the investigators suggest in the December 14, 2004, *Proceedings of the National Academy of Sciences USA.* *—JR Minkel*

HUBERT STADLER/CORBIS (*top*); BURKE/TRIOLO PRODUCTIONS/PICTUREARTS/BRAND X (*bottom*); ILLUSTRATION BY MATT COLLINS

DEMENTIA

## Cardio Therapy for the Mind

BRAIN SMART: Keeping blood pressure and cholesterol levels low may be more effective than drugs in treating mixed dementia.

**Treating the mind** could literally start with therapies for the heart. As many as 20 percent of the 6.8 million Americans with dementia actually suffer from a combination of Alzheimer's disease and vascular dementia, which results when high cholesterol, blood pressure, smoking or other factors damage blood vessels in the brain. Kenneth Langa of the University of Michigan Health System and his colleagues reviewed all medical studies linked to this mixed dementia from the past 10 years. They found that memory-preserving anti-Alzheimer's drugs led to at best a slight improvement or slowed decline of cognitive function. On the other hand, heart-protecting therapies had significant benefits for mixed dementia. They conclude that treatments against cardiovascular risk factors, especially high blood pressure, may be more effective than expensive memory drugs in protecting brain function. The report appears in the December 15 *Journal of the American Medical Association.* *—Charles Q. Choi*

NANOTECH

## Golden Zipper

**As a means for sensing** proteins and other molecular tasks, researchers have managed to link nanoparticles to DNA. Now investigators at the University of Dortmund in Germany have figured out how to unlink them under normal physiological conditions, potentially offering a controllable way to construct complicated nanostructures or devices that interact with the body. The researchers synthesized batches of two different single DNA strands, then attached each strand to its own 20-nanometer-wide gold particle. A longer third strand of DNA binds to both shorter sequences, linking the gold particles together. The trick is that the third strand has an extra region that hangs loose. In the December 3 *Angewandte Chemie International Edition,* they describe how they separated the gold particles by introducing a fourth strand that binds to the third strand's loose end and unzips it from the gold particles; reconnection simply meant introducing the naked third strand again. —*JR Minkel*

COMPUTING

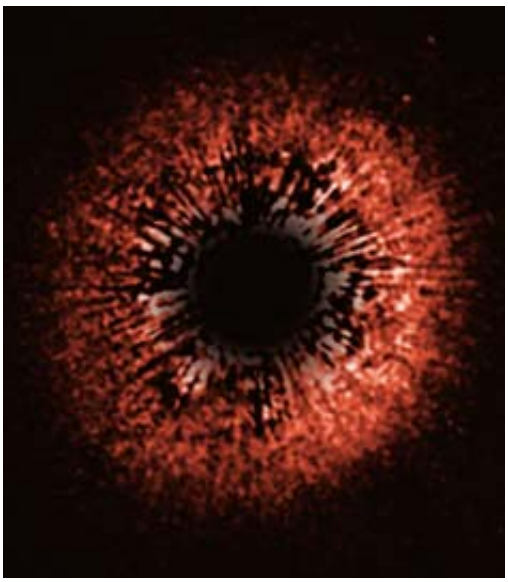
## Shrinking Memory

**Ferroelectric random-access** memory, or FRAM, relies on lining up dipoles (separated charges) to represent 0 and 1, giving it the speed of RAM and, notably, the ability to retain data without power. Unfortunately, FRAM does not offer as much storage space: dipoles in small ferroelectric bits do not all line up easily. Now University of Arkansas researchers may have discovered a way to shrink ferroelectric bits. They simulated the behavior of dipoles in nanosize disks and rods of perovskite, a promising ferroelectric material, and found that they spontaneously twist into left- and right-handed spiral shapes. Such vortices mark a new phase in ferroelectric materials, and because they are tiny and interact weakly with one another, they can be packed very closely together, which could increase their memory density 100,000 times. Read the group's report in the December 9, 2004, *Nature.* —*JR Minkel*

ASTRONOMY

## Planet-Making 101

**New snapshots of dusty disks** provide unprecedented looks at how worlds evolve around stars akin to our sun. The Hubble Space Telescope captured a picture of starlit asteroidal and cometary debris encircling the yellow dwarf star HD 107146. At 30 million to 250 million years old, it is a younger cousin of our 4.5-billion-year-old sun, but based on the size of its ring, astronomers believe HD 107146 will end up with a wildly different system, perhaps with giant worlds in eccentric orbits. This discovery, announced December 9, joins those from the Spitzer Space Telescope, which examined six sunlike stars known to have planets and discerned disks of rubble leftover from the formation of these worlds. These findings should help refine models of planetary development and guide future planet-hunting missions, such as the NASA Space Interferometry Mission. —*Charles Q. Choi*



DEBRIS DISK (*in false color*) encircles the young yellow dwarf star HD 107146, 88 light-years from Earth. The disk marks an early stage of planetary formation.

NASA, ESA, C. BEICHMAN (JPL), D. ARDILA (JHU) AND J. KRIST (STScI/JPL)

BRIEF POINTS

- **Sleep less, weigh more? Compared with people who sleep eight hours, five-hour snoozers produce 15 percent more gherlin, a hunger hormone, and 15 percent less leptin, an appetite suppressor.**

  *PLoS Medicine,* December 7, 2004

- **Anatomy shaper: the driving force behind the evolution of the *Homo* species from *Australopithecus* may have been the ability to run long distances, for hunting or scavenging across Africa's vast savannas.**

  *Nature,* November 18, 2004

- **Detecting neutrinos typically means looking for faint flashes that occur when the ghostly particles collide with atoms in water. An astrophysicist suggests that Jupiter's icy moon Europa could serve as a sensor of neutrinos a million times more energetic than those that can be caught on Earth.**

  Physicsweb.org, November 25, 2004

- **Antibodies from narcoleptic people induced a narcolepsylike symptom in the muscle of mice, suggesting that an autoimmune process plays a role in the sleep-wake disorder.**

  *Lancet,* December 11, 2004

# Abducted!

## Imaginary traumas are as terrifying as the real thing

By MICHAEL SHERMER

**In the wee hours** of the morning on August 8, 1983, while I was traveling along a lonely rural highway approaching Haigler, Neb., a large craft with bright lights overtook me and forced me to the side of the road. Alien beings exited the craft and abducted me for 90 minutes, after which time I found myself back on the road with no memory of what transpired inside the ship. I can prove that this happened because I recounted it to a film crew shortly afterward.

When alien abductees recount to me their stories, I do not deny that they had a real experience. But thanks to recent research by Harvard University psychologists Richard J. McNally and Susan A. Clancy, we now know that some fantasies are indistinguishable from reality, and they can be just as traumatic. In a 2004 paper in *Psychological Science* entitled "Psychophysiological Responding during Script-Driven Imagery in People Reporting Abduction by Space Aliens," McNally, Clancy and their colleagues report the results of a study of claimed abductees. The researchers measured heart rate, skin conductance and electromyographic responses in a muscle that lifted the eyebrow—called the left lateral (outer) frontalis—of the study participants as they relived their experiences through script-driven imagery. "Relative to control participants," the authors concluded, "abductees exhibited greater psychophysiological reactivity to abduction and stressful scripts than to positive and neutral scripts." In fact, the abductees' responses were comparable to those of post-traumatic stress disorder (PTSD) patients who had listened to scripts of their actual traumatic experiences.

**In 1983, in rural Nebraska, I was abducted by aliens.**

The abduction study was initiated as a control in a larger investigation of memories of sexual abuse. In his book *Remembering Trauma* (Harvard University Press, 2003), McNally tracks the history of the recovered memory movement of the 1990s, in which some people, while attempting to recover lost memories of childhood sexual molestation (usually through hypnosis and guided imagery), instead created false memories of abuse that never happened. "The fact that people who believe they have been abducted by space aliens respond like PTSD patients to audiotaped scripts describing their alleged abductions," McNally explains, "underscores the power of belief to drive a physiology consistent with actual traumatic experience." The vividness of a traumatic memory cannot be taken as evidence of its authenticity.

The most likely explanation for alien abductions is sleep paralysis and hypnopompic (on awakening) hallucinations. Temporary paralysis is often accompanied by visual and auditory hallucinations and sexual fantasies, all of which are interpreted within the context of pop culture's fascination with UFOs and aliens. McNally found that abductees "were much more prone to exhibit false recall and false recognition in the lab than were control subjects," and they scored significantly higher than normal on a questionnaire measuring "absorption," a trait related to fantasy proneness that also predicts false recall.

My abduction experience was triggered by sleep deprivation and physical exhaustion. I had just ridden a bicycle 83 straight hours and 1,259 miles in the opening days of the 3,100-mile nonstop transcontinental Race Across America. I was sleepily weaving down the road when my support motor home flashed its high beams and pulled alongside, and my crew entreated me to take a sleep break. At that moment a distant memory of the 1960s television series *The Invaders* was inculcated into my waking dream. In the series, alien beings were taking over the earth by replicating actual people but, inexplicably, retained a stiff little finger. Suddenly the members of my support team were transmogrified into aliens. I stared intensely at their fingers and grilled them on both technical and personal matters.

After my 90-minute sleep break, the experience represented nothing more than a bizarre hallucination, which I recounted to *ABC's Wide World of Sports* television crew filming the race. But at the time the experience was real, and that's the point. The human capacity for self-delusion is boundless, and the effects of belief are overpowering. Thanks to science we have learned to tell the difference between fantasy and reality. SA

*Michael Shermer is publisher of* Skeptic *(www.skeptic.com) and author of* The Science of Good and Evil.

BRAD HINES

# Performance without Anxiety

**Fear of reinforcing negative stereotypes, Claude Steele finds, hampers the ability to succeed. The idea is now central in affirmative action and job discrimination fights** By SALLY LEHRMAN

**In experiments starting in 1939,** American social psychologists Kenneth Clark and Mamie Clark discovered that black children preferred to play with dolls that were white. Their data helped to convince the Supreme Court in *Brown v. Board of Education* that separate education was inherently unequal.

Now civil-rights lawyers are turning once again to psychology as a way to reveal the powerful hidden barriers created by modern-day bias. In battles over issues from affirmative action to workplace discrimination, educators, political theorists and activists are relying on Stanford University social psychologist Claude Steele's studies on "stereotype threat" to argue for policies that might make access to jobs and education fair for everyone.

TIMOTHY ARCHIBALD

## CLAUDE STEELE: FIGHTING IDENTITY THREAT

- **Formulated the concept of stereotype threat, which is international: the same 15-point gap in IQ between U.S. blacks and whites exists between castelike minorities and majority populations in Japan, India and Israel.**
- **On workplace discrimination: "In many cases, it's not prejudice at the heart of the situation. It's the interplay of stereotype threat, which causes tension and lack of trust."**

The roots of the concept trace back to a phenomenon Steele explored shortly after he began his academic career at the University of Utah in the 1970s. It turned on the potent consequences of being judged negatively, even when the only basis was one's membership in a group. Researchers telephoned residents and made negative characterizations, such as "people in your community are lousy drivers." In separate calls later, the subjects who had been insulted were more likely than others to agree to help a food co-op. They were trying to maintain a positive self-image, Steele concluded, and it didn't matter if the food co-op had nothing to do with driving skills. The results also demonstrated that threats to self-image in turn affect behavior.

Steele extended the concept to stereotypes after joining the faculty of the University of Michigan at Ann Arbor in 1987. While advising a program for minority students, he noticed that although these young people had enrolled with the same SAT scores as others, their grades trailed those of white students and they dropped out in much higher proportions. The trend still holds true across the country: In the 1990s proportionately one fifth more blacks left college than whites. When they did graduate, their grade-point averages were two thirds of a letter grade lower.

Steele wondered if the Michigan students suffered from a kind of self-image threat, so with colleagues Joshua Aronson and Steven Spencer, he designed a series of studies. They gave sophomores matched by SAT scores a frustrating section of the Graduate Record Examination. When first told that the test evaluated verbal ability, the black students scored a full standard deviation lower on average. But when the researchers described it as a study of problem-solving techniques unimportant to academic achievement, the scores for blacks leaped to the same level as those for whites.

Mathematically accomplished women react comparably, Steele has observed. When given a difficult set of problems, they assumed their math abilities were under fire and scored significantly lower than men. But when told that gender could not affect scores, the women did as well as equally skilled men. Steele developed the theory of stereotype threat—that is, when people are challenged in an area they care deeply about, such as intellectual ability, the fear of confirming negative stereotypes can hurt their performance.

Social psychologists rapidly accepted the idea and even identified stereotype threat in groups not typically associated with bias. When experimenters told white golfers that the quality of their game would reflect "natural athletic ability" instead of their strategic intellectual prowess, their performance was much worse than that of black players. White male students' performance was similarly depressed when they took a math test in which Asian-Americans were said to do better. Internalized self-doubt could be eliminated as the cause, Steele and his colleagues concluded, because white men are not typically susceptible to worries about collective inferiority.


SUPPORTERS of affirmative action rallied outside the U.S. Supreme Court in 2003. Concepts such as stereotype threat played a key role in arguments.

But everyone feels marginalized at one time or another, so Steele hopes his ideas can foster more understanding and help to integrate society better. He has struggled with the problem since youth. His activist parents, an interracial couple who married in 1944, trained their children in nonviolent resistance and brought them to demonstrations against segregation in Chicago's parks. But even though Steele grew up in a fairly integrated setting, he could go to the skating rink or swimming pool only on certain days and was never allowed at his maternal grandparents' house. Such circumstances left the young Steele angry and mystified: "If my life had been a more exclusively black world, some of these issues may not have been as central."

Modest and reserved, the 59-year-old Steele isn't someone you might expect to find at the front of a social movement. As a scientist, he worries that his research will be misinterpreted to serve political aims. But like it or not, stereotype threat has become central to the debate on standardized tests in college admissions and, some predict, could take on an equally crucial role in criminal justice and other civil-rights issues.

In the closely watched University of Michigan affirmative action case, Steele's testimony underlined the need for admissions officers to look beyond test scores. "His research was part of the picture we were painting—that race matters for a variety of reasons in today's America," says Marvin Krislov, general counsel for the university. In June 2003 the Supreme Court decided that diversity was critical to effective higher education.

Even so, Steele would like to move the discussion of race away from affirmative action. "It distracts from some of the more profound inequalities in American society," he says. Disparities in academic tracking, discipline and resources limit intellectual achievement from a child's very first day in school, he argues. And silent, psychological cues impede success as well. When schools relegate ethnic studies to special programs, for instance, students' identities are marginalized in tandem, Steele asserts. Or when a teacher starts talking about "white males," those students begin to feel threatened and uncomfortable.

Even efforts to improve diversity may backfire if they are seen as "remedial." Instead schools and employers can remove the internal barriers that stereotypes produce by creating a setting that makes them unimportant. A critical factor is diverse numbers, Steele now says. "Critical mass gives people a sense of identity safety," he explains, and protects against the threat of assumptions based on race or gender.

Steele's work will most likely become a significant tool for understanding how race affects people's lives and opportunities, says legal theorist Charles J. Ogletree, Jr. Ogletree expects stereotype threat to become a central theme in studies at the new institute on race and justice he will be directing at Harvard University. "I think it's the cornerstone of a new field of expertise that will help us think through and resolve problems of race at a much grander scale than ever before," Ogletree asserts.

With a laugh, Steele predicts it will take a whole village of scientists to fully understand the process. In testing, for instance, other influences may swamp stereotype threat. "That's why I think it's exciting—it's important and powerful but not very well understood," Steele remarks. He believes the phenomenon, diffuse throughout society, affects everything from white self-segregation to minority self-limitation. "Stereotype threat is a first attempt to characterize these processes," he explains. "You hope people make some sense out of it and use it." SA

*Sally Lehrman is based in Montara, Calif.*

TERU IWASAKI *AP Photo*

CLOSE RELATIONSHIP has evolved between humans and *Helicobacter pylori,* the bacterium that can cause inflammation in the stomach and duodenum (*red*) but may actually protect the esophagus (*green*). Researchers believe the organisms exchange complex signals with human cells.

# An Endangered Species in the Stomach

Is the decline of *Helicobacter pylori,* a bacterium living in the human stomach since time immemorial, good or bad for public health?

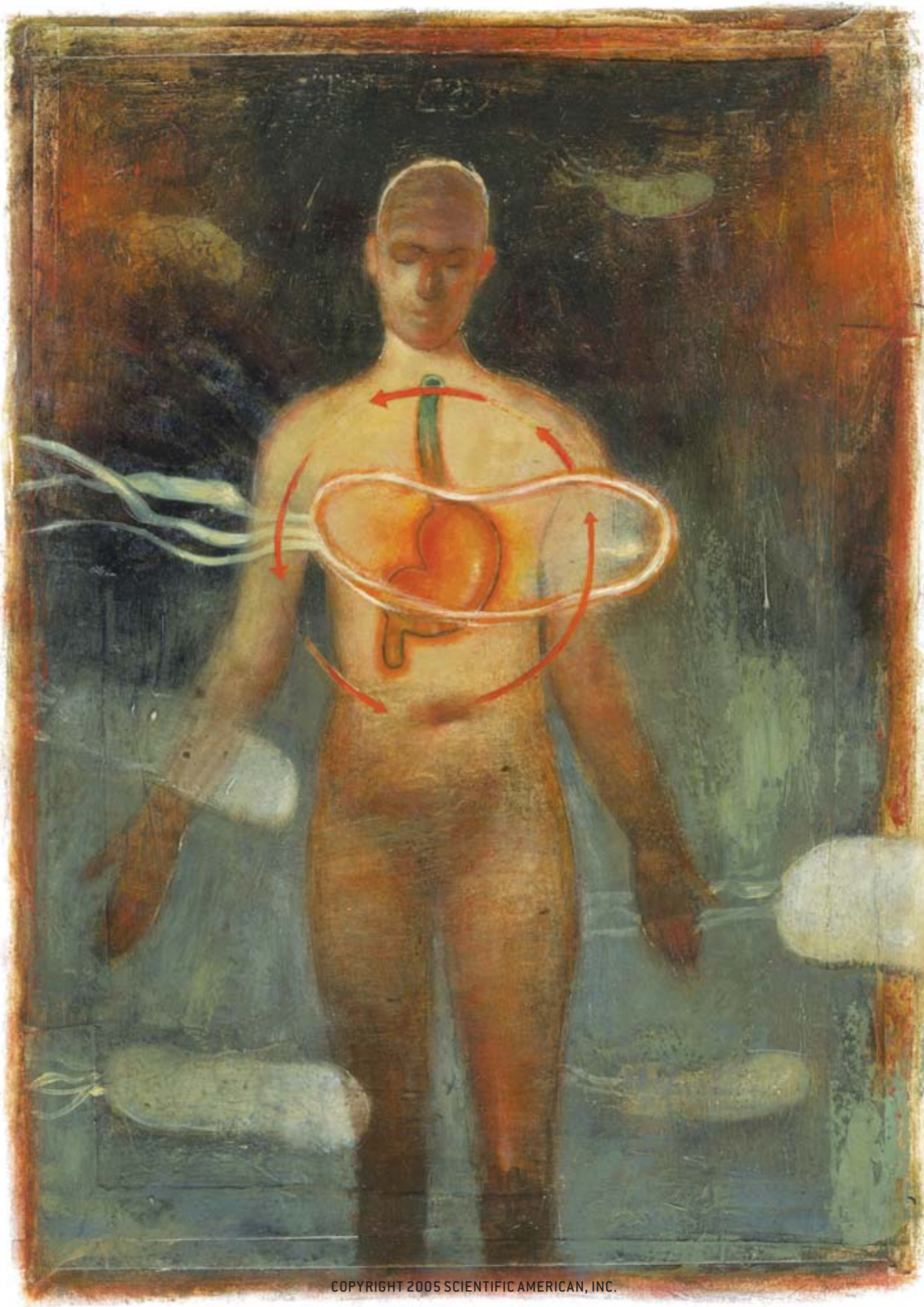
By Martin J. Blaser

*Helicobacter pylori* is one of humanity's oldest and closest companions, and yet it took scientists more than a century to recognize it. As early as 1875, German anatomists found spiral bacteria colonizing the mucus layer of the human stomach, but because the organisms could not be grown in a pure culture, the results were ignored and then forgotten. It was not until 1982 that Australian doctors Barry J. Marshall and J. Robin Warren isolated the bacteria, allowing investigations of *H. pylori*'s role in the stomach to begin in earnest. Over the next decade researchers discovered that people carrying the organisms had an increased risk of developing peptic ulcers—breaks in the lining of the stomach or duodenum—and that *H. pylori* could also trigger the onset of the most common form of stomach cancer [see "The Bacteria behind Ulcers," by Martin J. Blaser; Scientific American, February 1996].

Just as scientists were learning the importance of *H. pylori,* however, they discovered that the bacteria are losing their foothold in the human digestive tract. Whereas nearly all adults in the developing world still carry the organism, its prevalence is much lower in developed countries such as the U.S. Epidemiologists believe that *H. pylori* has been disappearing from developed nations for the past 100 years thanks to improved hygiene, which blocks the transmission of the bacteria, and to the widespread use of antibiotics. As *H. pylori* has retreated, the rates of peptic ulcers and stomach cancer have dropped. But at the same time, diseases of the esophagus—including acid reflux disease and a particularly deadly type of esophageal cancer—have increased dramatically, and a wide body of evidence indicates that the rise of these illnesses is also related to the disappearance of *H. pylori.*

The possibility that this bacterium may actually protect people against diseases of the esophagus has significant implications. For instance, current antibiotic treatments that eradicate *H. pylori* from the stomach may have to be reconsidered to ensure that the benefits are not outweighed by any potential harm. To fully understand *H. pylori*'s effects on health, researchers must investigate the complex web of interactions between this remarkable microbe and its hosts. Ultimately, the study of *H. pylori* may help us understand other bacteria that colonize the human body, as well as the evolutionary processes that allow humans and bacteria to develop such intimate relations with one another.

JOSEPH DANIEL FIEDLER



## A Diverse Bacterium

AS SOON AS scientists began investigating *H. pylori,* it became clear that strains isolated from different individuals are highly diverse. (A variety of strains can also be found in a single stomach.) Although the strains are identical in appearance, their genetic codes vary greatly. Researchers have determined the complete genomic DNA sequences for two separate *H. pylori* strains; each has a single small chromosome of approximately 1.7 million nucleotides, comprising about 1,550 individual genes. (In comparison, *Escherichia coli*—a bacterium inhabiting the intestines—has about five million nucleotides, and humans have about three billion.) Remarkably, about 6 percent of the *H. pylori* genes are not shared between the two strains, and even the shared genes have a significant amount of variation in their nucleotide sequences.

This level of diversity within a species is extraordinary. The genetic differences between humans and chimpanzees—two distinct species—are tiny compared with the differences among *H. pylori* strains: 99 percent of the nucleotide sequences in the human and chimp genomes are identical. The substantial variation in *H. pylori*'s genome suggests that either the bacteria have existed for a very long time as a species or that any particular variant is not so much better adapted to the human stomach as to outcompete all the others. In fact, both statements are true.

My laboratory has identified two particular types of variation. In 1989 we created a library of *H. pylori* genes by inserting selected fragments of the bacterium's DNA into cells of *E. coli*. The *E. coli* cells can then produce the proteins encoded by the *H. pylori* genes. We screened the resulting *E. coli* samples using blood serum from a person (me!) who carried *H. pylori* in his stomach; because my immune system had been exposed to the bacterium, the antibodies in my serum would be able to recognize some of the organism's protein products. The first sample that my antibodies recognized contained a gene that we now call *cagA*, which encodes the CagA protein. This was the first *H. pylori* gene found in some but not all strains of the bacterium. Later research indicated that people infected with *H. pylori* strains bearing the *cagA* gene have a higher risk of acquiring peptic ulcer disease or stomach cancer than people with strains lacking the gene.

We now know that *cagA* is part of a region in the *H. pylori* chromosome that also contains genes encoding proteins that form a type IV secretion system (TFSS). Bacterial cells assemble these systems to export large, complex molecules into host cells; for example, *Bordetella pertussis,* the bacterium that causes whooping cough, uses a TFSS to introduce its toxin into the cells of the human respiratory tract. In 2000 research groups in Germany, Japan, Italy and the U.S. determined that several of the *H. pylori* genes near *cagA* encode TFSS proteins that assemble into a structure analogous to a miniature hypodermic needle [*see box on opposite page*]. This structure injects the CagA protein into the epithelial cells that line the human stomach, which explains why my body produced antibodies to the protein.

After CagA enters an epithelial cell, enzymes in the host chemically transform the protein, allowing it to interact with several human proteins. These interactions ultimately affect the cell's shape, secretions and signals to other cells. Strains of *H. pylori* bearing the *cagA* gene cause more severe inflammation and tissue injury in the stomach lining than do strains without the gene. These differences may explain the increased disease risk in people carrying the *cagA* strains.

In the late 1980s Timothy Cover, then a postdoctoral fellow working with me, began to study some *H. pylori* strains that caused large holes, called vacuoles, to form in epithelial cells in culture. We showed that the active agent was a toxin, dubbed VacA, encoded by a gene that we named *vacA*. In addition to forming the vacuoles, VacA turns off the infection-fighting white blood cells in the stomach, diminishing the immune response to *H. pylori*. Unlike *cagA*, *vacA* is present in every *H. pylori* strain, but because the gene's sequence varies substantially, only some of the strains produce a fully functional toxin. John C. Atherton, a visiting postdoctoral fellow from England, found four major variations in *vacA:* two (m1 and m2) in the middle region of the gene and two (s1 and s2) in the region that encodes the protein's signal sequence, which enables the protein to move through cell membranes. Subsequent studies showed that the s1 variation could be divided into at least three subtypes: s1a, s1b and s1c.

*H. pylori* strains with both the m1 and s1 variations produce the most damaging form of the VacA toxin. Thus, it is

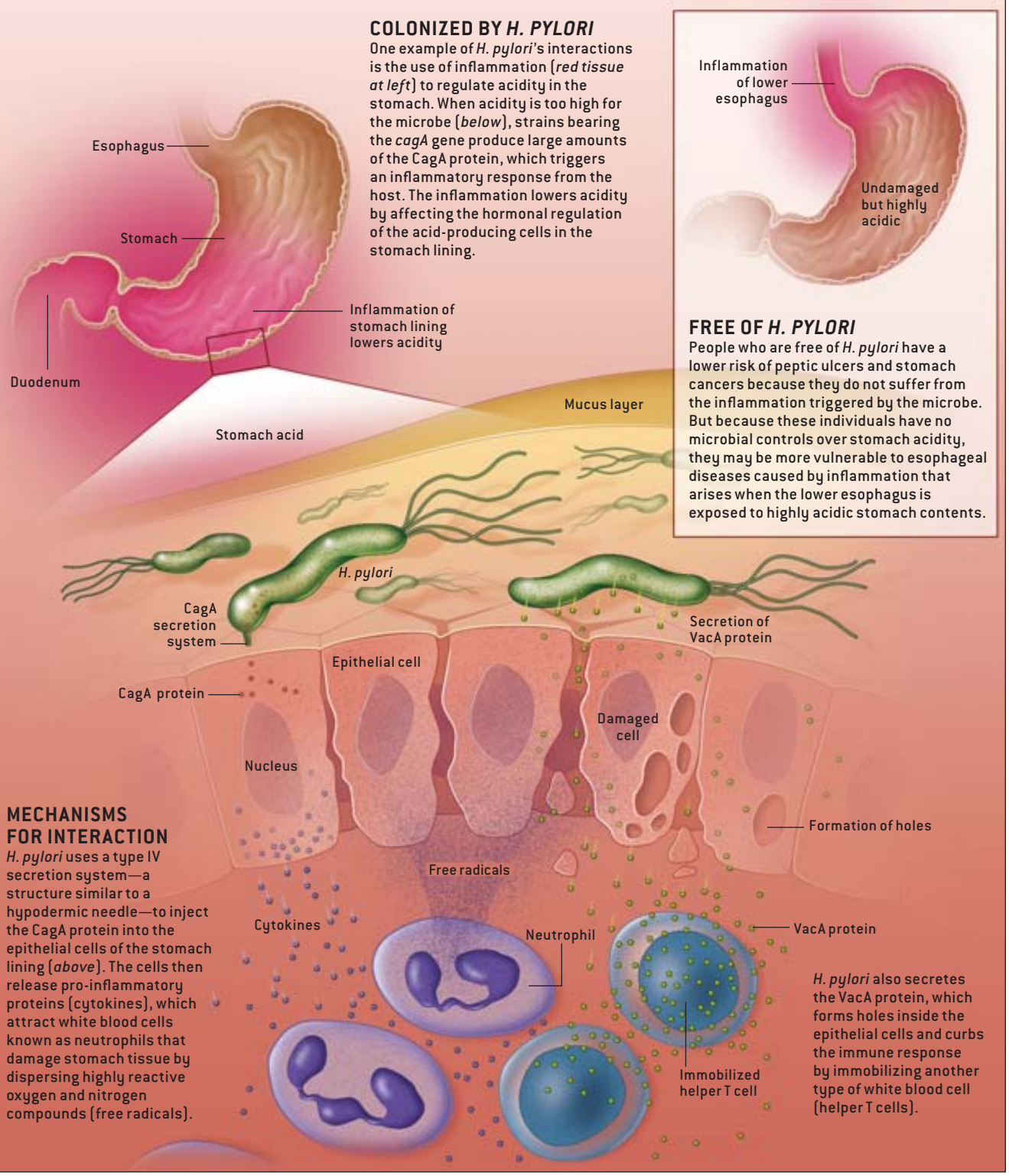
The prevalence of *Helicobacter pylori* is much lower in developed countries such as the U.S.

## Overview/*A Microbe's Effects*

- Although *Helicobacter pylori* has long colonized human stomachs, improved sanitation and antibiotics have drastically cut the bacterium's prevalence in developed countries over the past century.
- People carrying *H. pylori* have a higher risk of developing peptic ulcers and stomach cancer but a lower risk of acquiring diseases of the esophagus, including a very deadly type of esophageal cancer.
- Studies of the interactions between *H. pylori* and humans may lead to better treatments for disorders of the digestive tract as well as a greater understanding of other bacteria that colonize the human body.

# INTERACTIONS IN THE STOMACH

*Helicobacter pylori* can persist in the human stomach for decades, causing continual damage despite the host's immune response. Researchers theorize that the microbes and host exchange signals in a negative feedback loop that moderates the tissue damage and maintains a stable environment for the bacteria.




## COLONIZED BY *H. PYLORI*

One example of *H. pylori*'s interactions is the use of inflammation (*red tissue at left*) to regulate acidity in the stomach. When acidity is too high for the microbe (*below*), strains bearing the *cagA* gene produce large amounts of the CagA protein, which triggers an inflammatory response from the host. The inflammation lowers acidity by affecting the hormonal regulation of the acid-producing cells in the stomach lining.

## FREE OF *H. PYLORI*

People who are free of *H. pylori* have a lower risk of peptic ulcers and stomach cancers because they do not suffer from the inflammation triggered by the microbe. But because these individuals have no microbial controls over stomach acidity, they may be more vulnerable to esophageal diseases caused by inflammation that arises when the lower esophagus is exposed to highly acidic stomach contents.

## MECHANISMS FOR INTERACTION

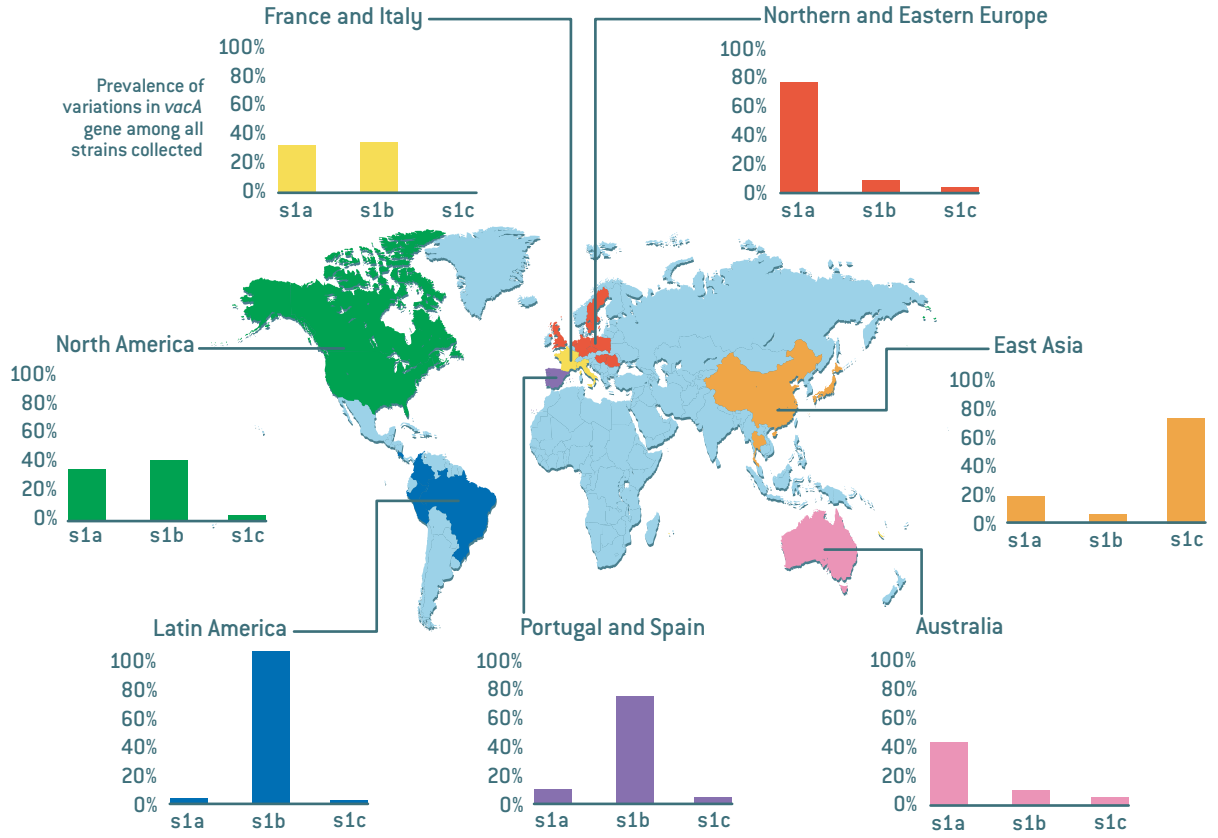
*H. pylori* uses a type IV secretion system—a structure similar to a hypodermic needle—to inject the CagA protein into the epithelial cells of the stomach lining (*above*). The cells then release pro-inflammatory proteins (cytokines), which attract white blood cells known as neutrophils that damage stomach tissue by dispersing highly reactive oxygen and nitrogen compounds (free radicals).

*H. pylori* also secretes the VacA protein, which forms holes inside the epithelial cells and curbs the immune response by immobilizing another type of white blood cell (helper T cells).

TAMI TOLPA

## A WORLD OF VARIATIONS

*H. pylori* is an ancient and genetically diverse organism, and the geographic distribution of its variant strains reflects the origins and migrations of its human hosts. The s1a variation of the *vacA* gene predominates in northern Europe, whereas the s1b and s1c variations prevail in the Mediterranean area and East Asia, respectively.




not surprising that strains bearing this genotype of *vacA*, combined with the *cagA* gene, are associated with the highest risk of stomach cancer. To make matters even more complicated, some people are more susceptible to these kinds of cancers because of variations in their own genes that enhance the inflammatory response to bacterial agents. The worst-case scenario is a person who carries the pro-inflammatory variations and is colonized with *H. pylori* strains containing the *cagA* gene and the s1/m1 *vacA* genotype. The collision of particularly aggressive *H. pylori* strains with particularly susceptible hosts appears to account for most cases of stomach cancer.


THE AUTHOR

*MARTIN J. BLASER* is one of the world's foremost experts on *Helicobacter pylori*. He is Frederick H. King Professor of Internal Medicine, chair of the department of medicine and professor of microbiology at New York University School of Medicine. Blaser previously worked at the University of Colorado, the Centers for Disease Control and Prevention, the Rockefeller University and Vanderbilt University. Since earning his M.D. at New York University in 1973, he has written over 400 original scientific articles and edited several books on infectious diseases. He is also president-elect of the Infectious Diseases Society of America.


## Tracing Migrations

ONCE SCIENTISTS HAD DISCOVERED ways to distinguish among the *H. pylori* strains that had been collected from around the world, they began to investigate whether strains circulating in different areas varied from one another. Working with Leen-Jan van Doorn of Delft Diagnostic Laboratory in the Netherlands, we found that variations in the *vacA* gene tended to cluster in certain geographic regions: s1c strains predominated in East Asia, s1a in northern Europe and s1b in the Mediterranean area [*see box above*].

My colleague Guillermo I. Perez-Perez and I were particularly interested in studying the *H. pylori* strains in Latin America because the results there could indicate when and how the bacteria arrived in the New World. We initially found that the Mediterranean strain, s1b, was by far the most common, suggesting that *H. pylori* was brought by Spanish and Portuguese settlers or African slaves. We realized, however, that these studies were conducted in Latin America's coastal cities, where the people have mixed European, African and Amerindian ancestries. Working with Maria Gloria Dominguez Bello of the Venezuelan Institute for Scientific Research, we analyzed stomach samples from a more indigenous Amazonian population—peo-

LUCY READING-IKKANDA

ple in Puerto Ayacucho, a market town on the Orinoco River in Venezuela—and found that most of the strains had the s1c genotype that is prevalent in East Asia. This work provided evidence that *H. pylori* had been transported across the Bering Strait by the ancestors of present-day Amerindians and thus has been present in humans for at least 11,000 years.

More recent collaborations with Mark Achtman, Daniel Falush and their colleagues at the Max Planck Institute for Infection Biology in Berlin have shown that all modern *H. pylori* strains can be traced to five ancient populations—two arising in Africa, two in western or central Eurasia and one in East Asia. In fact, the genetic variations of *H. pylori* can be used to trace human settlement and migration patterns over the past 60,000 years. Because *H. pylori* is so much more genetically diverse than *Homo sapiens,* the bacteria can better elucidate the history of population movements than can studies of human mitochondrial DNA (the most commonly used marker for such investigations). As researchers attempt to clock the migrations of our species, the mitochondrial studies may provide the hour hand, but the genetic sequences of *H. pylori* may offer a more accurate minute hand.

The genetic variations of *H. pylori* can be used to trace human settlement and migration patterns.

## A Microbial Extinction

HUMANS ARE THE ONLY HOSTS for *H. pylori,* and the spread of the bacterium involves mouth-to-mouth or feces-to-mouth transmission. The geographic differences in *H. pylori* infection rates—much lower in the developed world than elsewhere—may be partly the result of improvements in sanitation in the U.S., Europe and other developed countries over the past century. But I believe that the widespread use of antibiotics has also contributed to the gradual elimination of *H. pylori*. Even short courses of antibiotics, given for any purpose, will eradicate the bacteria in some recipients. In developing countries where antibiotics are less commonly used, 70 to 100 percent of children become infected with *H. pylori* by the age of 10, and most remain colonized for life; in contrast, fewer than 10 percent of U.S.-born children now carry the organism. This difference represents a major change in human microecology.

Furthermore, the disappearance of *H. pylori* may be a sentinel event indicating the possibility of other microbial extinctions as well. *H. pylori* is the only bacterium that can persist in the acidic environment of the human stomach, and its presence can be easily determined by tests of blood, stool, breath or stomach tissue. But other body sites, such as the mouth, colon, skin and vagina, have complex populations of indigenous organisms. If another common bacterium were disappearing from these tissues, we would not have the diagnostic tools to detect its decline.

What are the consequences of *H. pylori*'s retreat? As noted, the incidences of both peptic ulcer disease (except those cases caused by aspirin and nonsteroidal anti-inflammatory agents such as ibuprofen) and stomach cancer are clearly declining in developed countries. Because these illnesses, especially stomach cancer, develop over many years, the drop in disease incidence has lagged several decades behind the decline in *H. pylori* infection, but the falloff is startling nonetheless. In 1900 stomach cancer was the leading cause of cancer death in the U.S.; by 2000 the incidence and mortality rates had fallen by more than 80 percent, putting them well below the rates for colon, prostate, breast and lung cancers. Substantial evidence indicates that the continuing extinction of *H. pylori* has played an important role in this phenomenal change. This is the good news.

At the same time, however, there has been an unexpected rise in the incidence of a new class of diseases involving the esophagus. Since the early 1970s, epidemiologists in the U.S., the U.K., Sweden and Australia have noted an alarming jump in esophageal adenocarcinoma, an aggressive cancer that develops in the inner lining of the esophagus just above the stomach. The incidence of this illness in the U.S. has been climbing by 7 to 9 percent each year, making it the fastest-increasing major cancer in the country. Once diagnosed, the five-year survival rate for esophageal adenocarcinoma is less than 10 percent.

Where are these terrible cancers coming from? We know that the primary risk factor is gastroesophageal reflux disease (GERD), a chronic inflammatory disorder involving the regurgitation of acidic stomach contents into the esophagus. More commonly known as acid reflux disease, GERD was not even described in the medical literature until the 1930s. Since then, however, its incidence has risen dramatically, and now the disorder is quite common in the U.S. and other western countries. GERD can lead to Barrett's esophagus, a premalignant lesion first described in 1950 by English surgeon Norman Barrett. The incidence of Barrett's esophagus is rising in tandem

NATURAL HABITAT of *H. pylori* is the layer of mucus that lines the human stomach.

PHOTO INSOLITE REALITE & V. GREMET/PHOTO RESEARCHERS, INC.

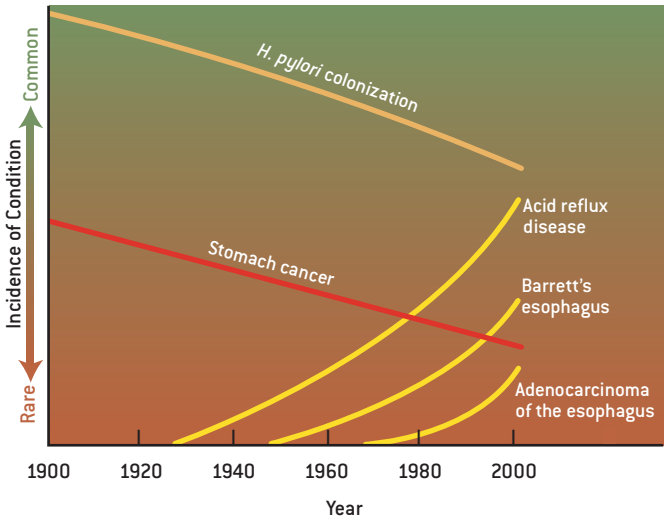
with that of GERD, and patients suffering from the condition have an increased risk of developing esophageal adenocarcinoma. It is becoming clear that GERD may initiate a 20- to 50-year process: in some cases, the disorder slowly progresses to Barrett's esophagus and then to adenocarcinoma, paralleling the gradual changes that lead to cancers in other epithelial tissues [*see illustration at right*]. But why are GERD and its follow-on disorders becoming more common?

The rise of these diseases has occurred just as *H. pylori* has been disappearing, and it is tempting to associate the two phenomena. When I began proposing this connection in 1996, I was greeted first by indifference and then by hostility. In recent years, though, a growing number of studies support the hypothesis that *H. pylori* colonization of the stomach actually protects the esophagus against GERD and its consequences. What is more, the strains bearing the *cagA* gene—that is, the bacteria that are most virulent in causing ulcers and stomach cancer—appear to be the most protective of the esophagus! In 1998, working with researchers from the National Cancer Institute, we found that people carrying *cagA* strains of *H. pylori* had a significantly decreased risk of developing adenocarcinomas of the lower esophagus and the part of the stomach closest to the esophagus. Then, in collaboration with investigators from the Cleveland Clinic and the Erasmus Medical Center in the Netherlands, we showed a similar correlation for both GERD and Barrett's esophagus. Independent confirmations have come from the U.K., Brazil and Sweden. Not all investigators have found this effect, perhaps because of differences in the methods of the studies. Nevertheless, the scientific evidence is now persuasive.

## A Theory of Interactions

HOW CAN COLONIZATION by *H. pylori* increase the risk of stomach diseases but protect against esophageal disorders? A possible explanation lies in the interactions between the bacterium and its human host. *H. pylori* has evolved into a most unusual parasite: it can persist in a stomach for decades despite causing continual damage and despite the host's immune response against it. This persistence requires that virtually all the "up-regulatory" events that cause inflammation in the stomach tissue must be balanced by "down-regulatory" events that prevent the damage from worsening too rapidly. There must be an equilibrium between microbe and host; otherwise, the host would die rather quickly, and the bacteria would lose their home before getting a chance to propagate to another person. But how can two competing forms of life achieve this equilibrium? My hypothesis is that the microbe and host must be sending signals to each other in a negative feedback loop.

Negative feedback loops are common in biology for the regulation of cellular interactions. Consider, for example, the feedback loop involving glucose and the regulatory hormone insulin. After you eat a meal, glucose levels in the bloodstream rise and the pancreas secretes insulin. The insulin causes glucose levels to fall, which signals the pancreas to reduce insulin secretion. By modulating the peaks and valleys in glucose levels, the system maintains a steady state called homeostasis. First described in the 19th century by French physiologist Claude Bernard, this concept has become the basis for understanding hormone regulation.




DECLINE of *H. pylori* in developed countries over the past 100 years has reduced the incidence of stomach cancer but may be triggering an upsurge in diseases of the esophagus. In some cases, acid reflux disease progresses to Barrett's esophagus (a premalignant lesion) and then to adenocarcinoma, a particularly deadly type of cancer. Because historical data on some disorders are incomplete, the plot lines show only general trends in disease incidence.

In essence, I took this idea one step further: the feedback relationship can involve microbial cells as well as host cells. Over the years, working with mathematicians Denise Kirschner of the University of Michigan at Ann Arbor and Glenn Webb of Vanderbilt University, our concepts of feedback have become more complex and encompassing. In our current formulation, the *H. pylori* population in a person's stomach is a group of extremely varied strains cooperating and competing with one another. They compete for nutrients, niches in the stomach and protection from stresses. Over the millennia, the long coevolution of *H. pylori* and *H. sapiens* has put intense selective pressure on both species. To minimize the damage from infection, humans have developed ways to signal to the bacteria, through immune responses and changes in the pressure and acidity in the stomach. And *H. pylori,* in turn, can signal the host cells to alleviate the stresses on the bacteria.

A good example of an important stress on *H. pylori* is the level of acidity in the stomach. Too much acid will kill the bacteria, but an extremely low level is not good either, because it would allow less acid-tolerant organisms such as *E. coli* to invade *H. pylori*'s niche. Therefore, *H. pylori* has evolved the ability to regulate the acidity of its environment. For example, strains bearing the *cagA* gene can use the CagA protein as a signaling molecule. When acidity is high, the *cagA* gene produces a relatively large amount of the protein, which triggers an inflammatory response from the host that lowers acidity by affecting the hormonal regulation of the acid-producing cells in the stomach lining. Low acidity, in contrast, curtails

LUCY READING-IKKANDA

the production of CagA and hence reduces the inflammation.

This negative feedback model helps us understand the health effects of *H. pylori,* which depend in large part on the intensity of the interactions between the bacteria and their hosts. The *cagA* strains substantially increase the risk of stomach cancer because they inject the CagA protein into the stomach's epithelial cells for decades, affecting the longevity of the host cells and their propensity to induce inflammation that promotes cancer. Strains lacking the *cagA* gene are much less interactive, so they do not damage the stomach tissues as severely. On the other hand, *cagA* strains effectively modulate acid production in the stomach, preventing acidity levels from rising too high. People who carry strains lacking the *cagA* gene have a weaker modulation of acidity levels, and people who are not colonized by *H. pylori* have no microbial controls at all. The resulting swings in stomach acidity may be central to the rise in esophageal diseases, which are apparently triggered by the exposure of the tissue to highly acidic stomach contents.

The absence of *H. pylori* may have other physiological effects as well. The stomach produces two hormones that affect eating behavior: leptin, which signals the brain to stop eating, and ghrelin, which stimulates appetite. Eradication of *H. pylori* with antibiotics tends to lower leptin and increase ghrelin; in one study, patients who had undergone treatment to eliminate *H. pylori* gained more weight than the control subjects did. Could changes in human microecology be contributing to the current epidemic of obesity and diabetes mellitus (an obesity-related condition) in developed countries? If this research were confirmed, the implications would be sobering. Doctors might need to reevaluate antibiotic treatments that rid the stomach of *H. pylori* (and remove critical bacteria from other parts of the body as well). Although some of the consequences of eradication may be for the better (for example, a reduced risk of stomach cancer) other effects may be for the worse. The balance between good and bad may well depend on the patient's age, medical history and genetic type.

## Probiotics

IF RESEARCHERS CONCLUDE that *H. pylori* would actually benefit some individuals, should physicians reintroduce the bacterium to these patients' stomachs? For more than 100 years, both medical scientists and laypersons have been searching for probiotics, microbes that can be ingested to aid human health. The earliest studies focused on the *Lactobacillus* species, the bacteria that make yogurt and many cheeses, but the effects of reintroduction were, at best, of marginal value. Researchers have largely failed to find any effective probiotics despite a century of trying.

One reason for this failure is the complexity and coevolution of the human microbiota, the organisms that share our bodies. Our microbiota are highly evolved for living within us and with each other. How likely is it that a newcomer, an unrelated strain of bacteria from outside the body, can successfully rechannel the pathways of interaction in a beneficial way? The existing organisms have survived strong and continuous selection, and this "home court advantage" usually enables them to reject and eliminate any strangers.

But a new day for probiotics may be coming. The key step will be gathering more knowledge of our indigenous microbiota and how they interact with us. I believe that complex interactions take place wherever microbes colonize our bodies (for example, in the colon, mouth, skin and vagina), but because of the array of competing organisms in those tissues, the relations are difficult to elucidate. *H. pylori,* though, largely excludes other microbes from the stomach. By the paradox of its great adaptation to humans and by the accident of its progressive disappearance during the 20th century, *H. pylori* may become a model organism for investigating human microecology.

**The study of *H. pylori* may help us understand other bacteria that colonize the human body.**

Once scientists fully catalogue the myriad strains of *H. pylori* and discover how each affects the host cells of the stomach, this research may give clinicians a whole new arsenal for fighting diseases of the digestive tract. In the future, a physician may be able to analyze a patient's DNA to determine his or her susceptibility to inflammation and genetic risks of acquiring different kinds of cancers. Then the doctor could determine the best mix of *H. pylori* strains for the patient and introduce the microbes to his or her stomach. What is more, researchers may be able to apply their knowledge of *H. pylori* to solve other medical problems. Just as the Botox nerve toxin produced by *Clostridium botulinum,* the bacterium that causes botulism, is now used for cosmetic surgery, the toxin VacA could become the basis for a novel class of drugs that suppress immune function. The study of our longtime bacterial companions offers a new avenue for understanding our own bodies and promises to expand the horizons of medical microbiology. SA

### MORE TO EXPLORE


**Dynamics of *Helicobacter pylori* Colonization in Relation to the Host Response.** Martin J. Blaser and Denise Kirschner in *Proceedings of the National Academy of Sciences USA,* Vol. 96, Issue 15, pages 8359–8364; July 20, 1999.

**Traces of Human Migrations in *Helicobacter pylori* Populations.** D. Falush, T. Wirth, B. Linz, J. K. Pritchard, M. Stephens, M. Kidd, M. J. Blaser, D. Y. Graham, S. Vacher, G. I. Perez-Perez, Y. Yamaoka, F. Mégraud, K. Otto, U. Reichard, E. Katzowitsch, X. Wang, M. Achtman and S. Suerbaum in *Science,* Vol. 299, pages 1582–1585; March 7, 2003.

***Helicobacter pylori* Persistence: Biology and Disease.** Martin J. Blaser and John C. Atherton in *Journal of Clinical Investigation,* Vol. 113, No. 3, pages 321–333; February 2004.

# Atom

BY JAKOB REICHEL

*Magnetic fields on a microchip can produce tiny, coherent clouds of atoms called Bose-Einstein condensates. The chips could have uses in ultraprecise sensors for aircraft and in quantum computing*

# Chips

ULTRACOLD CLOUD OF ATOMS levitates in the magnetic field produced near the surface of a simple microchip, in this artist's conception.

A century after its conception, quantum mechanics continues to be a disturbing theory. It tells us to think of all matter as waves, and yet in all objects that surround us these matter waves are far too small to be seen. Although the quantum laws are thought to be valid for objects of all sizes—from elementary particles to the universe as a whole—we do not usually see matter waves or any other quantum behavior in our everyday world.

In some subtle way, which physicists still do not completely understand, quantum mechanics conceals its strange effects when many particles interact in a disordered manner or when temperature rises much above absolute zero—that is, whenever things get a little bit complicated, as they usually do in the macroscopic world. As a result, quantum phenomena tend to be associated only with the world of elementary particles and with abstract thought experiments, such as the famous but mysterious Schrödinger's cat, which exists in a quantum state that is simultaneously alive and dead.

Recently, however, this picture has started to change. Physicists are learning to preserve the weirdness of quantum mechanics on larger and larger scales and to observe it in increasingly direct ways. One particularly beautiful example of this trend was the achievement of a Bose-Einstein condensate (BEC) of atoms in 1995. In a BEC, hundreds of thousands of atoms gather in the same quantum-mechanical state. Their individual matter waves all become exactly superposed. Because the resulting giant matter wave contains so many atoms, it is easy to observe: once a BEC is there, it takes hardly more than a video camera to see that matter has a wavy nature!

This unprecedented accessibility of matter waves has created a veritable BEC boom. Hundreds of researchers, theorists and experimentalists alike, who used to work in quite diverse subfields of physics, have turned their attention to the new topic. Over the past few years, BEC studies have given fresh experimental life to many quantum effects that formerly were considered very remote and inaccessible in practice. In this sense, BEC research has made quantum phenomena become more real, like a rock you can directly see and kick instead of something talked about in the abstract.

If BECs are easy to observe, creating them used to be a daunting task: the phase transition from a classical (nonquantum) atomic vapor to a condensate occurs at an extremely low temperature—usually less than a millionth of a degree above absolute zero. To achieve this temperature, the atoms must be isolated in a vacuum cell, suspended in free space by magnetic fields, and chilled by laser cooling and another technique called evaporative cooling [*see box on page 51*]. The slightest uncontrolled interaction with the room-temperature world around them would destroy the atoms' fragile quantum state. Thus, in the 50 or so research labs that are now able to produce BECs, the tiny cloud of ultracold atoms is usually surrounded by several tons of high-tech equipment. Ultrahigh-vacuum components, meticulously cleaned according to "voodoo" recipes, produce the world's best vacua and protect the atoms from the violent collisions that occur in room-temperature gases such as the air around us.

ATOM CHIP in the lab of Jörg Schmiedmayer at the University of Heidelberg traps a cloud of cold lithium atoms above its surface. The mirror image of the atom cloud is visible in the chip's shiny gold-coated gallium arsenide surface.

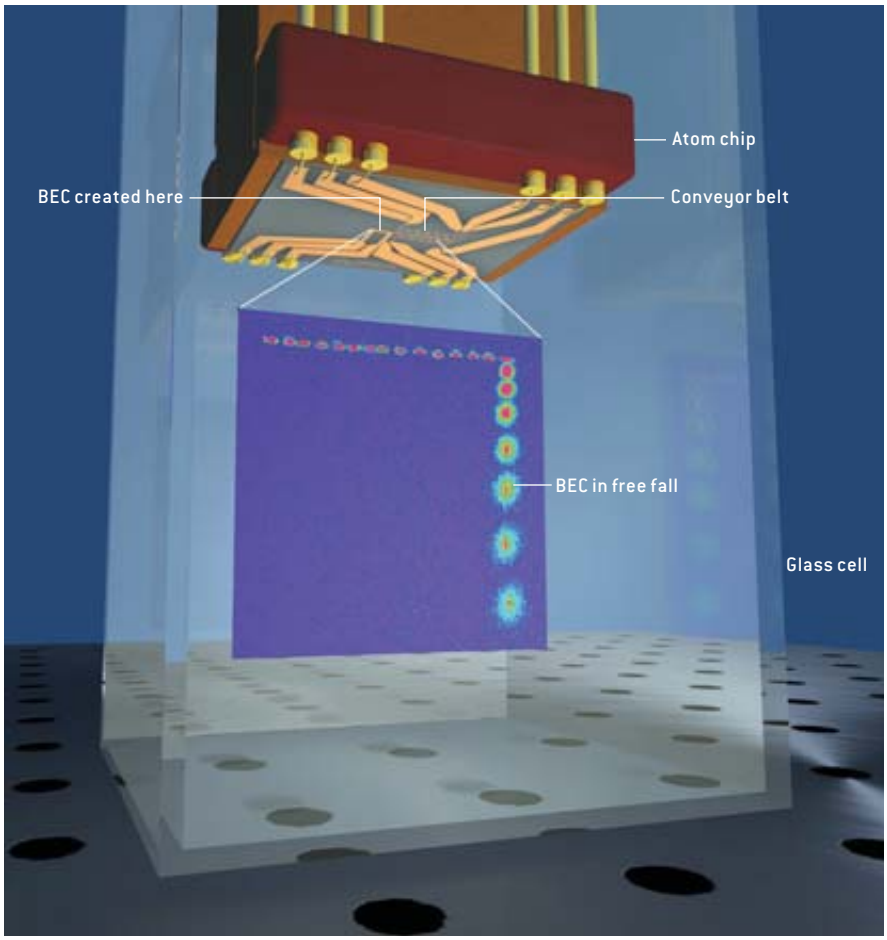
A key technique in all these experiments is magnetic trapping—the art of levitating atoms in free space with the help of magnetic fields. Evaporative cooling can work only in a trap, and magnetic traps are the ones that work best with this cooling technique. Furthermore, the stronger the trap (the more tightly the atoms are squeezed into a small volume), the faster and more efficient the cooling. Consequently, BEC researchers got accustomed to surrounding their vacuum cells with powerful but cumbersome electromagnets. To get the strongest magnetic compression, they developed heavy, water-cooled coils, often made from sturdy refrigerator tubing and consuming many kilowatts of electric power. Designing and operating these magnetic traps accounted for a significant part of the effort in BEC experiments.

In view of this experimental complexity, many found it hard to imagine that BECs could be employed in real-world applications, such as proposed portable rotation sensors, which might one day allow aircraft or submarines to navigate with unheard-of precision. Re-

KENN BROWN (*preceding pages*); JÖRG SCHMIEDMAYER (*this page*)

## Overview/*Atom Chips*

- Physicists are learning to preserve the weirdness of quantum mechanics on larger scales, which makes these phenomena easier to observe and to apply. Bose-Einstein condensates (BECs) are one such phenomenon, in which the wavy nature of matter is apparent.
- The magnetic fields on a microchip can hold a cloud of atoms suspended in a vacuum at a temperature just above absolute zero to create a BEC. Such "atom chips" are smaller than conventional magnetic traps, consume a thousandth as much power, operate much faster and require a less perfect vacuum.
- Atom chips could have applications as ultraprecise sensors for aircraft or marine navigation and for building quantum computers.




ATOMIC CONVEYOR BELT can transport and precisely position a Bose-Einstein condensate (BEC). The conveyor belt is the square-tooth wire structure in the center of the chip, which produces a series of magnetic wells whose position depends on the phase of the currents in the wires. The series of images (*purple square*) was taken while the conveyor transported the condensate over a distance of 1.6 millimeters along the chip surface. After the transport, the BEC was released into free fall. The shape it expanded to was characteristic of a BEC, demonstrating that the fragile condensate state survived the transport. (The chip structure and glass cell were added to the image to clarify the position of the conveyor.)

cently some remarkable developments have changed this state of affairs. In particular, we can now trap, move and manipulate the atoms with the help of microchips. A portable quantum laboratory, such as would be needed for the sensor applications, is no longer a wild dream but a very concrete research goal.

## A Magnetic Landscape

HOW CAN A MICROCHIP hold and control a cloud of atoms suspended near its surface? The answer is by taking advantage of the magnetic fields it naturally creates. Microchips such as the ones found in computers contain a complex array of thousands of microscopic wires. Currents flowing through these wires produce a magnetic field. Usually nobody cares about this field—at any macroscopic distance from the chip surface, the field is immeasurably small. Very near the wires, however, the field grows at a rate inversely proportional to the distance. Within 100 microns of the chip surface, the field forms the magnetic trap that suspends the atom cloud in free space. Because the atoms are so close to the wires, less than one watt of electric power is enough to operate this magnetic trap—it could easily be run off the battery of a laptop computer. Compare this with the kilowatts that were needed in the traditional magnetic traps.

Better still, the trap is much stronger than the conventional, coil-based ones, and it can create a BEC in less than a second. Coil-based traps rarely take less than half a minute to create a condensate. This increased speed is important because experiments on BECs typically need to be repeated hundreds of times to build up good statistics for a range of experimental conditions. Every single run requires the creation of a fresh BEC, needing a batch of atoms to be loaded and trapped and cooled all the way from well above room temperature to nearly absolute zero. It also makes a big difference for the rotation sensor, where higher speed directly translates into higher precision (because it reduces noise).

The increased speed simplifies the BEC apparatus quite dramatically because the vacuum can have 100 times as much residual gas in it. The problem with a poor vacuum is that the stray remaining particles steadily deplete the cloud of trapped atoms by colliding with them, thereby knocking them out of the magnetic trap. When the cooling proceeds faster, it is okay to have more of these stray particles in the system because they have less time to do their damage. So the vacuum technology can be much simpler: the vacuum for a chip BEC need hardly be better than that inside a television tube. Thus, miniaturizing the magnetic trap allows other parts of the apparatus to be miniaturized, too.

In spite of these advantages, at first it seems outrageous to try to store a BEC—thought to be the coldest object in the universe—within a hundred microns of a room-temperature surface (that of the microchip). Such a surface constantly emits infrared radiation, which can transfer heat to anything that is nearby. Who would store ice cubes near a radiator? Consequently, the first chip-trap proposal, put forward by a group at the California Institute of Technology in 1995, involved cooling the entire chip to near absolute zero using a bulky and expensive liquid-helium refrigerator. My own group wanted to preserve the appealing simplicity of the chip approach and chose in 1997 to work at room temperature and hope for the best.

THEODOR W. HÄNSCH

Fortunately, our ultracold atom clouds are very unlike ice cubes. A solid object such as an ice cube is a very efficient absorber of heat radiation. The gaseous atoms, however, absorb radiation only at certain sharply defined wavelengths, so the gas absorbs hardly any of the heat radiated by the chip. Today we know that all thermal interactions are negligibly weak at a distance of 100 microns and do no harm on the timescale of a BEC experiment.

When the idea of a chip trap first came up, shortly after the first BECs had been produced in 1995, a few tricky problems had to be solved before the dream could come true. First, of course, a trapping chip had to be designed and built. Learning how to do this was an enormously rewarding experience for me. I have always been impressed with the incredible pace of progress in the microelectronics industry, which faces new challenges every year but implacably overcomes them, one by one, to keep up its rate of miniaturization. As a cold-atom physicist, I had only a vague idea of the technologies behind this progress. Now I became involved with it. Talking to specialists in that field, consulting books and Web sites, I found out about thin-film hybrid devices, which feature gold conductors on little ceramic chips and can be used for atom trapping. I also learned to appreciate the vast technological culture of the microelectronics industry that usually stays behind the scenes, although we all use the electronics, from TV sets to notebook computers, that result from it.

Having learned how a trapping chip could be manufactured, my colleagues and I at the Max Planck Institute of Quantum Optics in Garching and the Ludwig Maximilian University in Munich were faced with the problem of loading the trap with atoms. Whether one is using a conventional coil-based system or an atom chip, before the atoms can be held in the purely magnetic trap, they must be cooled to microkelvin temperature in a magneto-optical trap (MOT). An essential element of a MOT is an array of six laser beams that bathe the atoms on all sides and from above and below. How can one implement a MOT when a chip surface gets in the way? The chip will inevitably block at least one of the beams, and the MOT no longer works.

The solution is to have a mirror coating on the chip reflect two of the beams [*see box on opposite page*]. If the lasers and the chip are oriented in the right way, the reflected beams can replace the blocked ones, and the MOT works again, producing a cloud of cold atoms right above the chip surface. A few additional details had to be taken into account (the polarization of the laser beams has to come out right), but the idea worked, and the system is now called a mirror-MOT, or a surface-MOT. Once the atoms are precooled in the mirror-MOT, loading them into the chip trap is easy: the MOT is switched off, and the current through the wires on the chip switched on. When this happens, most of the atom cloud finds itself trapped in the chip's magnetic field.

In 1998 graduate student Wolfgang Hänsel, quantum-optics wizard Theodor W. Hänsch and I employed this technique for trapping and cooling atoms in the first demonstration of an atom chip at the Max Planck Institute. Still, many researchers were skeptical about the future of the new technique for producing BECs, mainly because the chip surface is so close to the trapped atoms. In the summer of 2001 my group and that of Claus Zimmermann at the University of Tübingen, also in Germany, proved the doubters wrong and independently created BECs using microchip traps. It was a remarkable coincidence that our groups reached this long-sought breakthrough within only a few days of each other. Zimmermann (who had also been a collaborator of Hänsch before moving to Tübingen) has called it an entanglement of ideas, referring to the famous quantum-physics phenomenon. More than a dozen laboratories around the world now use atom chips for BEC experiments.

**It seems OUTRAGEOUS to store the coldest object in the universe SO CLOSE to a room-temperature surface.**

The basic atom chip requires only two or three wires in a simple arrangement to form a magnetic trap. But much more is possible thanks to another advantage of the technique—maybe the most important one: from its microelectronics ancestors, the atom chip inherits all the benefits of microfabrication technology. We can lay out the wires in any desired pattern, going around curves and meandering paths and even across one another. When currents travel through these wire arrangements, they produce a complex magnetic landscape for the atoms to explore, opening fantastic possibilities for atom manipulation.

For example, my group in Munich demonstrated a BEC "conveyor belt," using a chip whose structure went well beyond that of a simple trap [*see illustration on preceding page*]. When the currents applied to the various wires are


THE AUTHOR

*JAKOB REICHEL* obtained his Ph.D. from the École Normale Supérieure (ENS) in Paris. In his thesis, he used a laser-cooling method to obtain then record-low temperatures. He returned to his native Germany in 1997 to work at the Max Planck Institute of Quantum Optics in Garching and the Ludwig Maximilian University in Munich. There, together with Theodor W. Hänsch, he established a small group that pioneered the use of microfabrication methods for cold-atom manipulation. In the summer of 2004 Reichel received a European Young Investigator award and took up a position at the ENS in Paris, where he is setting up a microtrap research group. Married with a baby son, he finds inspiration playing the viola in a string quartet with good friends.

# COOLING A GAS OF ATOMS

Hot gas atoms behave a lot like hard little balls—they are very classical, or nonquantum. But every atom actually has a quantum wave packet that is spread out over a small region. For hot atoms, the wave packet is tiny, but it gets larger as an atom cools down. A Bose-Einstein condensate (BEC) forms when the gas is so cold and dense that the wave packets become large enough to overlap. Then the atoms all pile up in the same quantum state—the same wave packet—merging into a unified, wavelike blob that is a Bose-Einstein condensate.

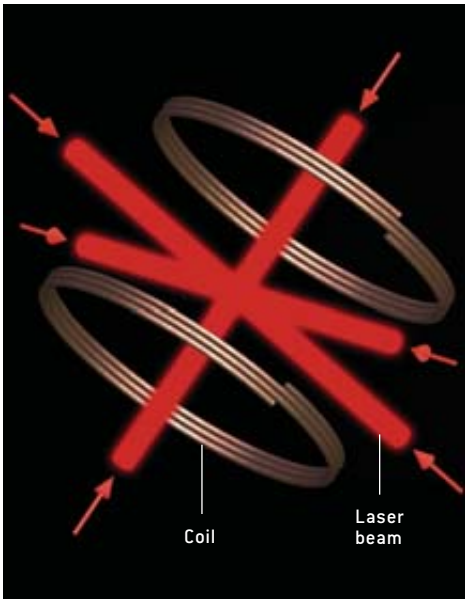
Producing a BEC takes a lot of equipment. The heart of a cold-atom experiment is a small glass box with some coils of wire around it. This cell is completely evacuated, producing in effect a superefficient thermos bottle. Next, a tiny amount of the desired gas is let in. Six laser beams intersect at one point inside the vacuum cell. The laser light need not be intense, so inexpensive diode lasers can often suffice, similar to those found in compact-disc players. At room temperature, the gas atoms irregularly fly through the cell with a speed of several hundred miles per hour. Where they happen to enter into one of the beams, the laser light starts to cool them down very abruptly. Additionally, a weak magnetic field from the wire coils conspires with the laser light to push the atoms toward the intersection of the six beams.

This clever combination of laser light and magnetic field, called a magneto-optical trap (MOT), was devised in 1987 by Jean Dalibard of École Normale Supérieure in Paris. David E. Pritchard of the Massachusetts Institute of Technology and Steven Chu of Stanford University created the first working MOT. Today the MOT is the workhorse of cold-atom physics, cooling gases of rubidium, sodium and many other atomic species to temperatures in the microkelvin range. Yet a MOT achieves only a fairly low density—the atoms are spaced too far apart for their wave functions to overlap. To get higher densities and still lower temperatures at the same time requires another mechanism. This is where evaporative cooling comes into play.

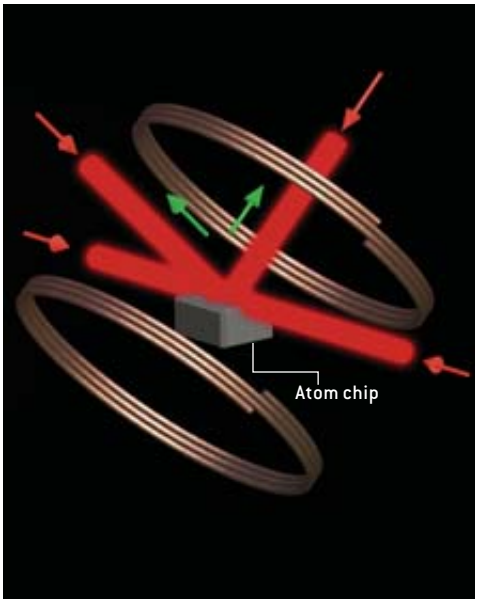
Evaporative cooling works because at every instant some particles in the gas are almost at rest, and others have much more than the average velocity. When those very fast atoms are removed, the remaining gas has a lower temperature. This is not a new idea: it is precisely how a cup of coffee cools when one blows on it.

To apply evaporative cooling to ultracold atoms requires some more refined equipment than a mouth and a pair of lungs, however. In BEC experiments, it is usually performed in a magnetic trap, which can be thought of as a deep bowl with immaterial walls. The most energetic atoms escape from the bowl. The walls of the bowl are steadily lowered so that hot atoms continue to escape, and the cooling process on the remaining ones keeps going.

An essential element of evaporative cooling is that the slower atoms left behind must redistribute their energy—a few of them end up with higher velocities (and are in turn removed from the trap as the evaporation proceeds), whereas the others become even slower and colder. This redistribution occurs through "good" collisions (as distinguished from "bad" collisions with surrounding atoms, which knock the desired atoms out of the trap). This is where the microchip traps weigh in: with small currents, they produce strong fields that compress the atoms more than standard traps, thereby increasing the rate of good collisions. —*J.R.*




In the standard MOT configuration (*left*), six laser beams (*red*) cross in the center of the magnetic field created by two coils. This configuration is difficult to use with a chip—the chip inevitably blocks one or more of the beams.




The solution (*right*) is to apply a mirror coating to the chip and to use only four beams instead of six. Reflection (*green arrows*) from the mirror coating provides the two remaining beams, and cold atoms are collected close to the chip surface.

KENN BROWN

modulated in an appropriate way, a series of potential wells moves across the chip surface. Regulating the currents controls the speed of transport and the distance from the surface. The condensate can be moved and positioned to within a few nanometers, or billionths of a meter. This BEC conveyor belt may become the backbone of more complex devices—for example, in quantum computing, which I discuss below.

But the BEC conveyor is just an initial example. Today researchers have only started to explore the possibilities offered by sculpting the magnetic field.

## Magnetic Tubes

WHEN THE CIRCUITRY takes the form of two or three wires running in parallel, the magnetic field forms a tube-like trap along which the atoms can move freely. The magnetic tube is the matter-wave analogue of an optical fiber: a matter waveguide. Light waves in a fiber move along the fiber axis, following its path around curves. Similarly, a condensate moves along a magnetic matter waveguide as a beam of matter. Several research teams have developed such guides (both on microchips and on larger systems) and the techniques for loading atoms into them.

The main application envisaged is atom interferometry. Any kind of interferometry involves combining two waves, resulting in a pattern of high and low amplitudes, or light and darkness. Most interferometry is carried out with laser beams because the technique relies on a property of laser light known as coherence, meaning there is one orderly wave associated with each beam. A traveling BEC is a lot like a laser beam in that it, too, is coherent. Bringing together two coherent atom beams produces interference—a pattern of "bright" spots (lots of atoms) and "dark" spots (with few).

Atom interferometers have evolved over the past decade from proof-of-principle experiments into sensors that compare favorably with other state-of-the-art sensors (although it could be a decade before they make the leap from the laboratory to real-world commercial applications). Most notably, they can be employed to measure rotation, gravity and local variations of gravity—quantities needed for navigation in ships and aircraft. For example, aircraft contain optical-fiber-based interferometers (called laser gyroscopes) to measure rotation—an indispensable supplement to the traditional compass. Gyroscopes based on atom interferometry may be several orders of magnitude more precise.

Important problems with chip-based systems remain to be solved, however. One is the development of coherent beam splitters, which divide a beam of atoms into two beams. A beam splitter is one of the main working parts in any interferometer. For the splitter to be coherent, every atom, like a kind of Schrödinger's cat, must go along both paths of the beam splitter at once—what the splitter does is to divide the atom's quantum wave function in two. In contrast, the chip beam splitters that have been demonstrated so far are more akin to fire hoses: they break apart the beam too abruptly, and each individual atom goes either left or right instead of going both ways at once. These "incoherent" devices cannot be used in an interferometer.

In July 2004 a collaboration between the group of Eric A. Cornell of JILA at the University of Colorado at Boulder and that of Mara Prentiss of Harvard University demonstrated an ingenious laser-based atom interferometer. The researchers created a BEC on an atom chip, and then with a laser pulse they split it into two coherent parts moving away from each other. Additional pulses brought the two parts back together to produce interference.

Beam splitters are not the only type of device to exhibit problems with matter waves. In 2002 Zimmermann's group and that of David E. Pritchard (one of the inventors of atom interferometry) at the Massachusetts Institute of Technology saw an unexpected effect when they released a condensate into a waveguide on a chip. Instead of seeing the condensate spread out and fill the guide to its end, like water settling in a long horizontal trough, they saw it start to spread but then stop and split up into fragments [*see box on opposite page*]. These little splashes of matter had been trapped in very shallow corrugations in the magnetic guide.

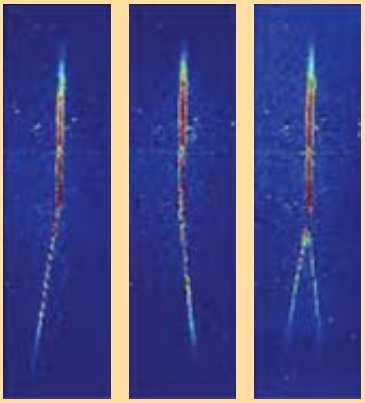
In March 2004 Alain Aspect and his co-workers at the Institute of Optics in Orsay, France, demonstrated with scanning electron microscopy and elegant analysis that roughness—small deviations of the wires from their ideal, straight form—is the cause of these corrugations in the magnetic waveguide. The tiny bumpiness of the wire is enough to make the current flow in little curves, distorting the magnetic field. These imperfections in the magnetic field have never been measured directly with conventional magnetic field probes. The BEC atoms turned out to be much more sensitive probes.

Another problem touches on much more fundamental effects. In experiments carried out so far, the BEC atoms are at least tens of microns from the chip surface. The fascinating quantum character of the atoms would be more pronounced in even smaller traps, but a side effect of making the magnetic traps smaller is that they will hold the atoms that much closer to the chip surface. At these tiny distances—less than one micron—the atoms will inevitably interact with the surface through a process known as the Casimir-Polder force. Indeed, in an experiment carried out in late 2003 by Vladan Vuletic, a young professor at M.I.T., a loss of atoms from the trap was observed when it was

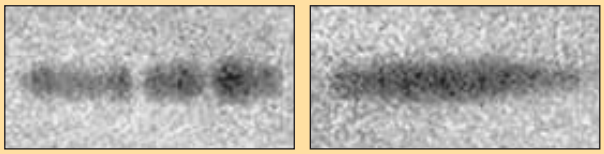
**Every atom, like a kind of SCHRÖDINGER'S CAT, must go along BOTH PATHS of the beam splitter at once.**

## CHALLENGES TO OVERCOME

**Matter waves are demanding travelers. If atom chips are to be used in applications, certain problems must be solved.**



Incoherence in an atom beam splitter means that each atom goes either left or right where the beam splits. For atom interferometry, researchers are striving to achieve a coherent version where every atom goes left and right simultaneously. At the left, we see an incoherent beam splitter controlling the flow of lithium atoms through its inverted Y shape.



Fragmentation of an atom cloud trapped in the magnetic field of a wire on a chip indicates that the magnetic potential is not completely smooth (*left*). The bumpiness of the magnetic waveguide is caused by microscopic roughness of the wires. When an atom cloud is trapped at exactly the same position but held by a purely optical trap that does not involve the chip wire, no fragmentation appears (*right*).

brought closer than about 1.5 microns to a nonconducting surface.

Finally, another effect that must be dealt with in smaller traps is the thermal magnetism of the chip surface. Imagine a disordered pile of little magnets in constant, chaotic movement. This is what a metal at room temperature looks like at submicron distances. At larger distances, the contributions all average to zero, which is why they have not been seen up until now. When the atoms are brought very close to the surface, however, they once again prove to be extremely sensitive probes. The thermal magnetism causes the magnetic trap to shake and move, and after some time the atoms are washed overboard. The effect was predicted in 1999 by Carsten Henkel of the University of Potsdam—a German theorist who became interested in atom chips soon after they were invented—and was experimentally verified in 2003 by Ed A. Hinds, now at Imperial College London, who had previously trapped cold atoms with other unconventional means such as videotape.

For applications where thermal magnetism is a problem, several solutions exist. The chip can be cooled with liquid nitrogen or even liquid helium, but this requirement complicates the apparatus considerably. As predicted by Henkel and demonstrated in 2003 by Cornell's team, the thermal magnetism is weaker in metals of higher resistivity. Thus, using titanium instead of copper or gold reduces the losses.

Waveguides, and their application in atom interferometers, exploit one particular aspect of the atom's quantum-mechanical nature: its wave character. Other quantum manifestations may lead to other, still more revolutionary applications. Today's star in the quantum scene is the quantum computer [see "Rules for a Complex Quantum World," by Michael A. Nielsen; Scientific American, November 2002]. This future device would exploit the superposition principle (another peculiar feature of the quantum world) to carry out certain types of computations much faster than any classical computer could do. A quantum computer functions by manipulating qubits, the quantum counterparts to bits. An ordinary, classical (nonquantum) logical bit can only be true or false, 1 or 0. The qubit, by contrast, can be in a superposition state corresponding to any mixture of true and false at the same time, like Schrödinger's cat in its mixture of alive and dead.

In a classical computer, computations corresponding to different bit states must be carried out one after the other. With qubits, they are elegantly performed all at the same time. It has been proven that for certain problems this feature makes a quantum computer fundamentally faster than any classical computer can ever be.

The favorite occupation of quantum physicists these days is to think of practical ways to make a quantum computer: with trapped ions, with large molecules, with electron spins—or maybe with BECs on atom chips. The idea is tempting because such a quantum chip seems so attractively similar to a traditional microelectronics chip and at the same time so radically new. Components such as the atom conveyor could be used to bring qubits together to interact in a controllable fashion.

Thus, the condensate on a chip is the beginning of a story. As so often occurs in science, the plot of the story is not known in advance, and the actors themselves are discovering it in little steps. As in the past, surprises will crop up—pleasant and unpleasant ones. Some obstacles will be removed; others will force researchers to change directions. Whatever we find out will help to bring the classical and quantum worlds still closer together on the stage of science. SA

### MORE TO EXPLORE


**Magnetic Chips and Quantum Circuits for Atoms.** E. Hinds in *Physics World,* Vol. 14, No. 7, pages 39–44; July 2001.

**Special section on Ultracold Matter.** *Nature,* Vol. 416, No. 6877, pages 205–246; March 14, 2002.

**Coherence with Atoms.** Mark A. Kasevich in *Science,* Vol. 298, No. 5597, pages 1363–1368; November 15, 2002.

Max Planck Institute of Quantum Optics (Garching) Microtrap Group: **www.mpq.mpg.de/~jar**

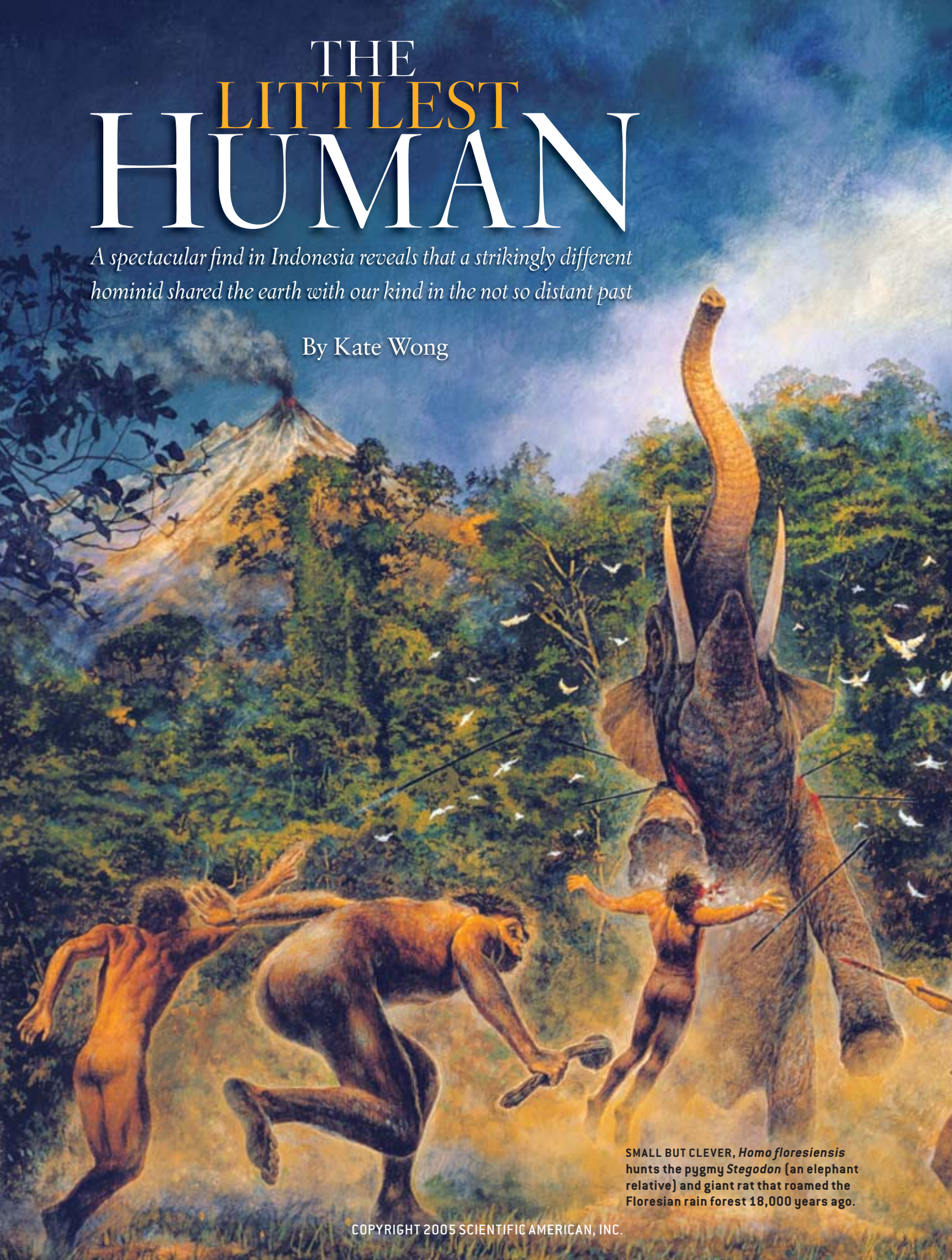
University of Heidelberg Atom Chip Group: **www.atomchip.org**


JÖRG SCHMIEDMAYER (*left*); WOLFGANG KETTERLE *Massachusetts Institute of Technology* (*right*)

# THE LITTLEST HUMAN

*A spectacular find in Indonesia reveals that a strikingly different hominid shared the earth with our kind in the not so distant past*

By Kate Wong



SMALL BUT CLEVER, *Homo floresiensis* hunts the pygmy *Stegodon* (an elephant relative) and giant rat that roamed the Floresian rain forest 18,000 years ago.

On the island of Flores in Indonesia, villagers have long told tales of a diminutive, upright-walking creature with a lopsided gait, a voracious appetite, and soft, murmuring speech.

They call it *ebu gogo,* "the grandmother who eats anything." Scientists' best guess was that macaque monkeys inspired the *ebu gogo* lore. But last October, an alluring alternative came to light. A team of Australian and Indonesian researchers excavating a cave on Flores unveiled the remains of a lilliputian human—one that stood barely a meter tall—whose kind lived as recently as 13,000 years ago.

The announcement electrified the paleoanthropology community. *Homo sapiens* was supposed to have had the planet to itself for the past 25 millennia, free from the company of other humans following the apparent demise of the Neandertals in Europe and *Homo erectus* in Asia. Furthermore, hominids this tiny were known only from fossils of australopithecines (Lucy and the like) that lived nearly three million years ago—long before the emergence of *H. sapiens*. No one would have predicted that our own species had a contemporary as small and primitive-looking as the little Floresian. Neither would anyone have guessed that a creature with a skull the size of a grapefruit might have possessed cognitive capabilities comparable to those of anatomically modern humans.

## Isle of Intrigue

THIS IS NOT THE FIRST TIME Flores has yielded surprises. In 1998 archaeologists led by Michael J. Morwood of the University of New England in Armidale, Australia, reported having discovered crude stone artifacts some 840,000 years old in the Soa Basin of central Flores. Although no human remains turned up with the tools, the implication was that *H. erectus,* the only hominid known to have lived in Southeast Asia during that time, had crossed the deep waters separating Flores from Java. To the team, the find showed *H. erectus* to be a seafarer, which was startling because elsewhere *H. erectus* had left behind little material culture to suggest that it was anywhere near capable of making watercraft. Indeed, the earliest accepted date for boat-building was 40,000 to 60,000 years ago, when modern humans colonized Australia. (The other early fauna on Flores probably got there by swimming

KAZUHIKO SANO (*preceding pages*)

**MODERN INDIAN ELEPHANT (*Elephas maximus*)**

## Overview/*Mini Humans*

- Conventional wisdom holds that *Homo sapiens* has been the sole human species on the earth for the past 25,000 years. Remains discovered on the Indonesian island of Flores have upended that view.
- The bones are said to belong to a dwarf species of *Homo* that lived as recently as 13,000 years ago.
- Although the hominid is as small in body and brain as the earliest humans, it appears to have made sophisticated stone tools, raising questions about the relation between brain size and intelligence.
- The find is controversial, however—some experts wonder whether the discoverers have correctly diagnosed the bones and whether anatomically modern humans might have made those advanced artifacts.

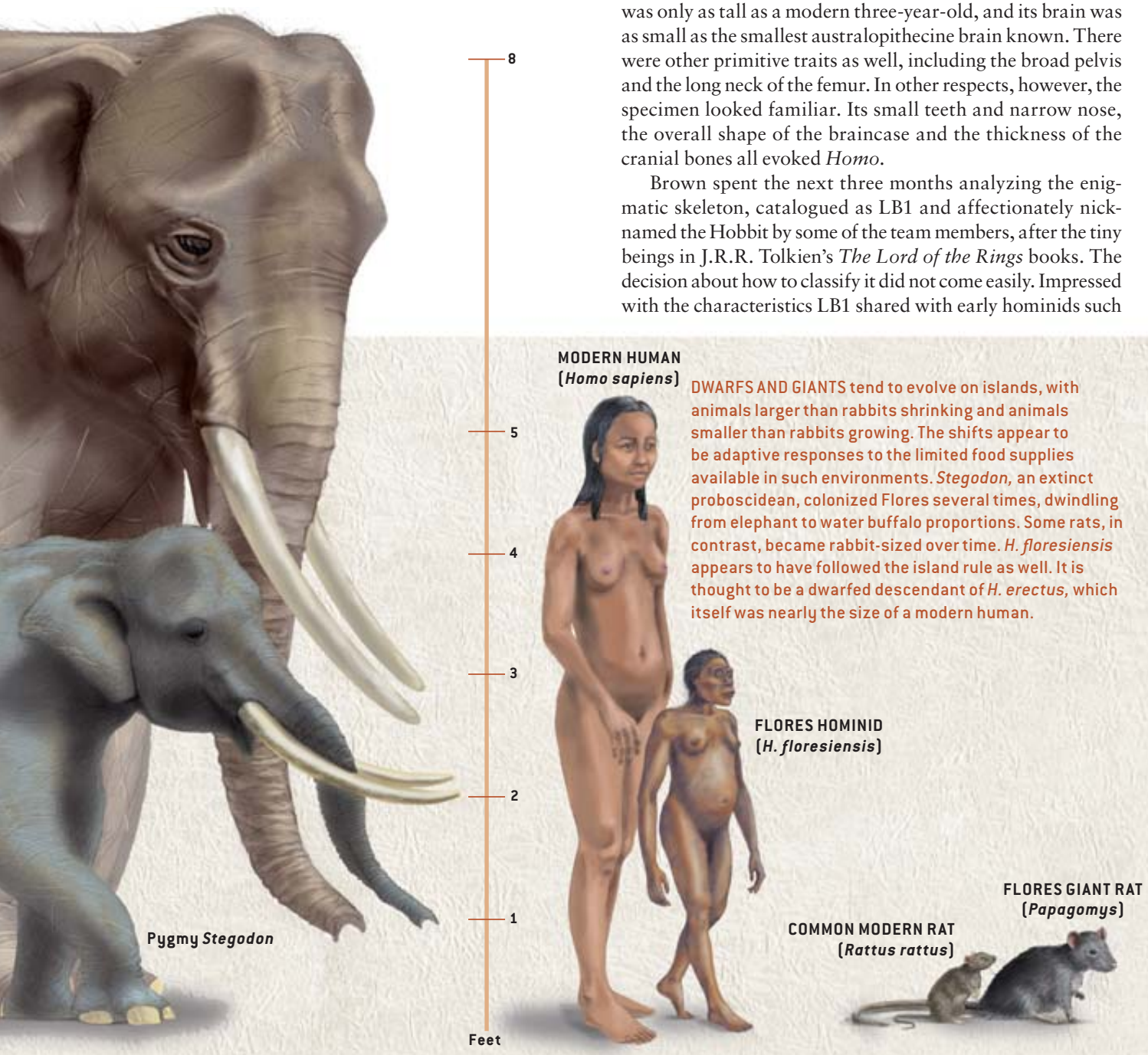
or accidentally drifting over on flotsam. Humans are not strong enough swimmers to have managed that voyage, but skeptics say they may have drifted across on natural rafts.

Hoping to document subsequent chapters of human occupation of the island, Morwood and Radien P. Soejono of the Indonesian Center for Archaeology in Jakarta turned their attention to a large limestone cave called Liang Bua located in western Flores. Indonesian archaeologists had been excavating the cave intermittently since the 1970s, depending on funding availability, but workers had penetrated only the uppermost deposits. Morwood and Soejono set their sights on reaching bedrock and began digging in July 2001. Before long, their team's efforts turned up abundant stone tools and bones of a pygmy version of an extinct elephant relative known as *Stegodon*. But it was not until nearly the end of the third season of fieldwork that diagnostic hominid material in the form of an isolated tooth surfaced. Morwood brought a cast of the tooth back to Armidale to show to his department colleague Peter Brown. "It was clear that while the premolar was broadly humanlike, it wasn't from a modern human," Brown recollects. Seven days later Morwood received word that the Indonesians had recovered a skeleton. The Australians boarded the next plane to Jakarta.

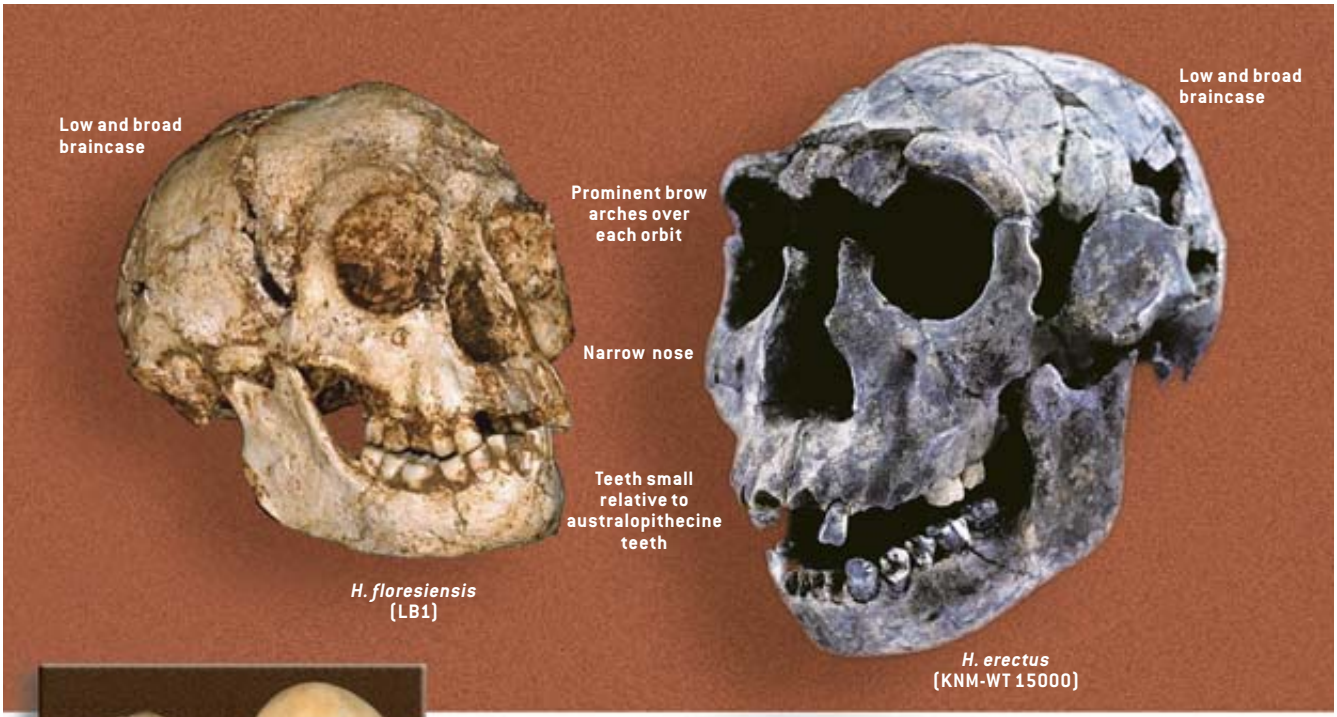
Peculiar though the premolar was, nothing could have prepared them for the skeleton, which apart from the missing arms was largely complete. The pelvis anatomy revealed that the individual was bipedal and probably a female, and the tooth eruption and wear indicated that it was an adult. Yet it was only as tall as a modern three-year-old, and its brain was as small as the smallest australopithecine brain known. There were other primitive traits as well, including the broad pelvis and the long neck of the femur. In other respects, however, the specimen looked familiar. Its small teeth and narrow nose, the overall shape of the braincase and the thickness of the cranial bones all evoked *Homo*.

Brown spent the next three months analyzing the enigmatic skeleton, catalogued as LB1 and affectionately nicknamed the Hobbit by some of the team members, after the tiny beings in J.R.R. Tolkien's *The Lord of the Rings* books. The decision about how to classify it did not come easily. Impressed with the characteristics LB1 shared with early hominids such

PORTIA SLOAN




DWARFS AND GIANTS tend to evolve on islands, with animals larger than rabbits shrinking and animals smaller than rabbits growing. The shifts appear to be adaptive responses to the limited food supplies available in such environments. *Stegodon,* an extinct proboscidean, colonized Flores several times, dwindling from elephant to water buffalo proportions. Some rats, in contrast, became rabbit-sized over time. *H. floresiensis* appears to have followed the island rule as well. It is thought to be a dwarfed descendant of *H. erectus,* which itself was nearly the size of a modern human.




SHARED FEATURES between LB1 and members of our own genus led to the classification of the Flores hominid as *Homo,* despite its tiny brain size. Noting that the specimen most closely resembles *H. erectus,* the researchers posit that it is a new species, *H. floresiensis,* that dwarfed from a *H. erectus* ancestor. *H. floresiensis* differs from *H. sapiens* in having, among other characteristics, no chin, a relatively projecting face, a prominent brow and a low braincase.

as the australopithecines, he initially proposed that it represented a new genus of human. On further consideration, however, the similarities to *Homo* proved more persuasive. Based on the 18,000-year age of LB1, one might have reasonably expected the bones to belong to *H. sapiens,* albeit a very petite representative. But when Brown and his colleagues considered the morphological characteristics of small-bodied modern humans—including normal ones, such as pygmies, and abnormal ones, such as pituitary dwarfs—LB1 did not seem to fit any of those descriptions. Pygmies have small bodies and large brains—the result of delayed growth during puberty, when the brain has already attained its full size. And individuals with genetic disorders that produce short stature and small brains have a range of distinctive features not seen in LB1 and rarely reach adulthood, Brown says. Conversely, he notes, the Flores skeleton exhibits archaic traits that have never been documented for abnormal small-bodied *H. sapiens*.

What LB1 looks like most, the researchers concluded, is a miniature *H. erectus*. Describing the find in the journal *Nature,* they assigned LB1 as well as the isolated tooth and an arm bone from older deposits to a new species of human, *Homo floresiensis*. They further argued that it was a descendant of *H. erectus* that had become marooned on Flores and evolved in isolation into a dwarf species, much as the elephantlike *Stegodon* did.

Biologists have long recognized that mammals larger than rabbits tend to shrink on small islands, presumably as an adaptive response to the limited food supply. They have little to lose by doing so, because these environments harbor few predators. On Flores, the only sizable predators were the Komodo dragon and another, even larger monitor lizard. Animals smaller than rabbits, on the other hand, tend to attain brobdingnagian proportions—perhaps because bigger bodies are more energetically efficient than small ones. Liang Bua has yielded evidence of that as well, in the form of a rat as robust as a rabbit.

But attributing a hominid's bantam size to the so-called island rule was a first. Received paleoanthropological wisdom holds that culture has buffered us humans from many of the selective pressures that mold other creatures—we cope with cold, for example, by building fires and making clothes, rather than evolving a proper pelage. The discovery of a dwarf hominid species indicates that, under the right conditions, humans can in fact respond in the same, predictable way that other large mammals do when the going gets tough. Hints that *Homo* could deal with resource fluxes in this manner came earlier in 2004 from the discovery of a relatively petite *H. erectus* skull from Olorgesailie in Kenya, remarks Richard Potts of the Smithsonian Institution, whose team recovered the bones. "Getting small is one of the things *H. erectus* had in its biological tool kit," he says, and the Flores hominid seems to be an extreme instance of that.

CHRISTIAN SIDOR *New York College of Osteopathic Medicine (H. sapiens)*; PETER BROWN *University of New England, Armidale* AND TIMEFORKIDS/KRT (*H. floresiensis*); DAVID BRILL (*H. erectus*)

## Curiouser and Curiouser

*H. FLORESIENSIS*'S teeny brain was perplexing. What the hominid reportedly managed to accomplish with such a modest organ was nothing less than astonishing. Big brains are a hallmark of human evolution. In the space of six million to seven million years, our ancestors more than tripled their cranial capacity, from some 360 cubic centimeters in *Sahelanthropus*, the earliest putative hominid, to a whopping 1,350 cubic centimeters on average in modern folks. Archaeological evidence indicates that behavioral complexity increased correspondingly. Experts were thus fairly certain that large brains are a prerequisite for advanced cultural practices. Yet whereas the pea-brained australopithecines left behind only crude stone tools at best (and most seem not to have done any stone working at all), the comparably gray-matter-impoverished *H. floresiensis* is said to have manufactured implements that exhibit a level of sophistication elsewhere associated exclusively with *H. sapiens*.

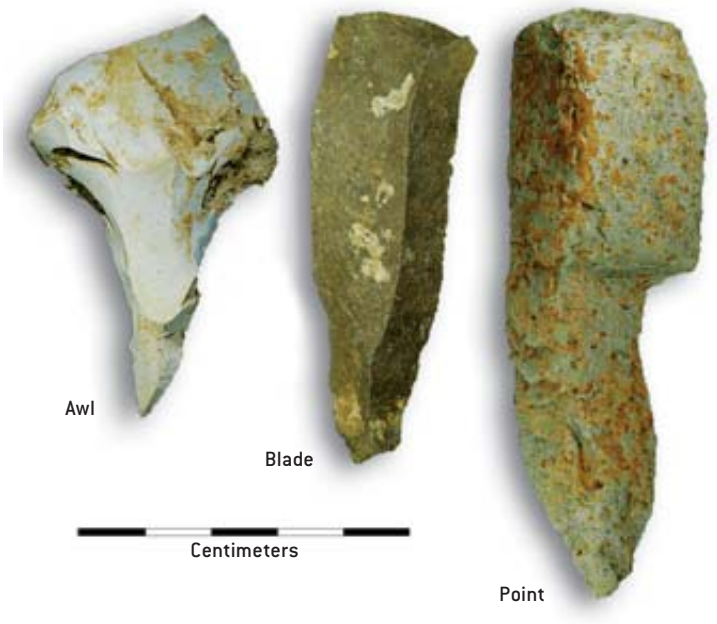
The bulk of the artifacts from Liang Bua are simple flake tools struck from volcanic rock and chert, no more advanced than the implements made by late australopithecines and early *Homo*. But mixed in among the pygmy *Stegodon* remains excavators found a fancier set of tools, one that included finely worked points, large blades, awls and small blades that may have been hafted for use as spears. To the team, this association suggests that *H. floresiensis* regularly hunted *Stegodon*. Many of the *Stegodon* bones are those of young individuals that one *H. floresiensis* might have been able to bring down alone. But some belonged to adults that weighed up to half a ton, the hunting and transport of which must have been a coordinated group activity—one that probably required language, surmises team member Richard G. ("Bert") Roberts of the University of Wollongong in Australia.

The discovery of charred animal remains in the cave suggests that cooking, too, was part of the cultural repertoire of *H. floresiensis*. That a hominid as cerebrally limited as this one might have had control of fire gives pause. Humans are not thought to have tamed flame until relatively late in our collective cognitive development: the earliest unequivocal evidence of fire use comes from 200,000-year-old hearths in Europe that were the handiwork of the large-brained Neandertals.

If the *H. floresiensis* discoverers are correct in their interpretation, theirs is one of the most important paleoanthropological finds in decades. Not only does it mean that another species of human coexisted with our ancestors just yesterday in geological terms, and that our genus is far more variable than expected, it raises all sorts of questions about brain size and intelligence. Perhaps it should come as no surprise, then, that controversy has accompanied their claims.

## Classification Clash

IT DID NOT TAKE LONG for alternative theories to surface. In a letter that ran in the October 31 edition of Australia's *Sunday Mail,* just three days after the publication of the *Nature* issue containing the initial reports, paleoanthropologist Maciej Henneberg of the University of Adelaide countered that




ADVANCED IMPLEMENTS appear to have been the handiwork of *H. floresiensis.* Earlier hominids with brains similar in size to that of *H. floresiensis* made only simple flake tools at most. But in the same stratigraphic levels as the hominid remains at Liang Bua, researchers found a suite of sophisticated artifacts—including awls, blades and points—exhibiting a level of complexity previously thought to be the sole purview of *H. sapiens.*

a pathological condition known as microcephaly (from the Greek for "small brain") could explain LB1's unusual features. Individuals afflicted with the most severe congenital form of microcephaly, primordial microcephalic dwarfism, die in childhood. But those with milder forms, though mentally retarded, can survive into adulthood. Statistically comparing the head and face dimensions of LB1 with those of a 4,000-year-old skull from Crete that is known to have belonged to a microcephalic, Henneberg found no significant differences between the two. Furthermore, he argued, the isolated forearm bone found deeper in the deposit corresponds to a height of 151 to 162 centimeters—the stature of many modern women and some men, not that of a dwarf—suggesting that larger-bodied people, too, lived at Liang Bua. In Henneberg's view, these findings indicate that LB1 is more likely a microcephalic *H. sapiens* than a new branch of *Homo*.

Susan C. Antón of New York University disagrees with that assessment. "The facial morphology is completely different in microcephalic [modern] humans," and their body size is normal, not small, she says. Antón questions whether LB1 warrants a new species, however. "There's little in the shape that differentiates it from *Homo erectus,*" she notes. One can argue that it's a new species, Antón allows, but the difference in shape between LB1 and *Homo erectus* is less striking than that between a Great Dane and a Chihuahua. The possibility exists that the LB1 specimen is a *H. erectus* individual with a pathological growth condition stemming

COURTESY OF MARK MOORE

from microcephaly or nutritional deprivation, she observes.

But some specialists say the Flores hominid's anatomy exhibits a more primitive pattern. According to Colin P. Groves of the Australian National University and David W. Cameron of the University of Sydney, the small brain, the long neck of the femur and other characteristics suggest an ancestor along the lines of *Homo habilis,* the earliest member of our genus, rather than the more advanced *H. erectus*. Milford H. Wolpoff of the University of Michigan at Ann Arbor wonders whether the Flores find might even represent an offshoot of *Australopithecus*. If LB1 is a descendant of *H. sapiens* or *H. erectus,* it is hard to imagine how natural selection left her with a brain that's even smaller than expected for her height, Wolpoff says. Granted, if she descended from *Australopithecus,* which had massive jaws and teeth, one has to account for her relatively delicate jaws and dainty dentition. That, however, is a lesser evolutionary conundrum than the one posed by her tiny brain, he asserts. After all, a shift in diet could explain the reduced chewing apparatus, but why would selection downsize intelligence?

Finding an australopithecine that lived outside of Africa—not to mention all the way over in Southeast Asia—18,000 years ago would be a first. Members of this group were thought to have died out in Africa one and a half million years ago, never having left their mother continent. Perhaps, researchers reasoned, hominids needed long, striding limbs, large brains and better technology before they could venture out into the rest of the Old World. But the recent discovery of 1.8 million-year-old *Homo* fossils at a site called Dmanisi in the Republic of Georgia refuted that explanation—the Georgian hominids were primitive and small and utilized tools like those australopithecines had made a million years before. Taking that into consideration, there is no a priori reason why australopithecines (or habilines, for that matter) could not have colonized other continents.

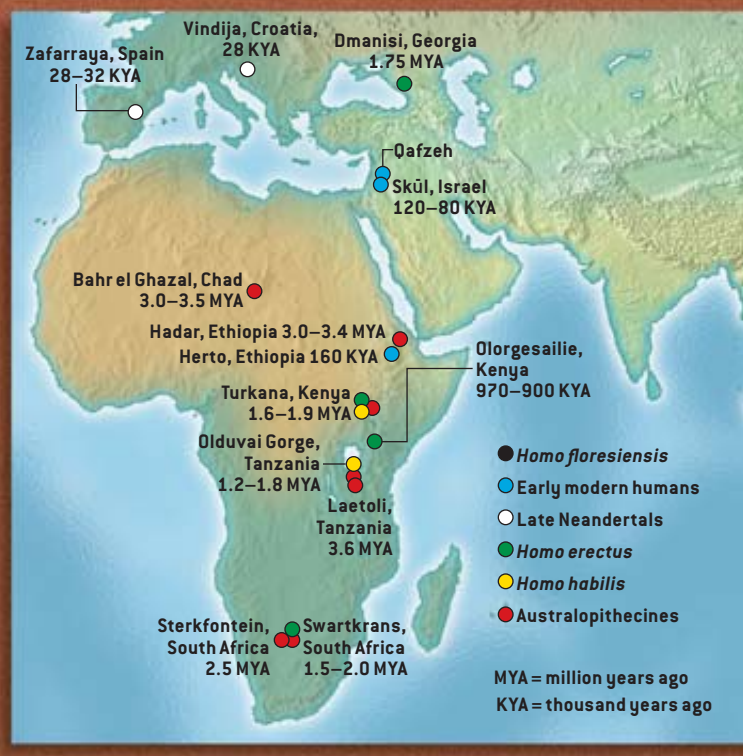
## Troubling Tools

YET IF *AUSTRALOPITHECUS* made it out of Africa and survived on Flores until quite recently, that would raise the question of why no other remains supporting that scenario have turned up in the region. According to Wolpoff, they may have: a handful of poorly studied Indonesian fossils discovered in the 1940s have been variously classified as *Australopithecus, Meganthropus* and, most recently, *H. erectus*. In light of the Flores find, he says, those remains deserve reexamination.

Many experts not involved in the discovery back Brown and Morwood's taxonomic decision, however. "Most of the differences [between the Flores hominid and known members of *Homo*], including apparent similarities to australopithecines, are almost certainly related to very small body mass," declares David R. Begun of the University of Toronto. That is, as the Flores people dwarfed from *H. erectus,* some of their anatomy simply converged on that of the likewise little australopithecines. Because LB1 shares some key derived features with *H. erectus* and some with other members of *Homo,* "the most straightforward option is to call it a new species of *Homo*," he remarks. "It's a fair and reasonable interpretation," *H. erectus* expert G. Philip Rightmire of Binghamton University agrees. "That was quite a little experiment in Indonesia."

Even more controversial than the position of the half-pint human on the family tree is the notion that it made those advanced-looking tools. Stanford University paleoanthropologist Richard Klein notes that the artifacts found near LB1

## Home of the Hobbit




Scholars were stunned a decade ago to learn that *H. erectus* might have survived on the island of Java in Indonesia until 25,000 years ago, well after the arrival of *H. sapiens* in the region and even after the disappearance of Europe's Neandertals. The recent revelation that a third hominid, dubbed *H. floresiensis,* lived in the area until just 13,000 years ago has proved even more provocative.

Archaeologists recovered the remains from a large limestone cave known as Liang Bua located in western Flores. No one knows exactly how humans first reached the island—they may have made the requisite sea crossings by boat, or they may have drifted over on natural rafts quite by accident.

Geographically, Javan *H. erectus* is a good candidate for the ancestor of *H. floresiensis.* But resemblances to specimens from Africa and the Republic of Georgia raise the question of whether *H. floresiensis* stemmed from a different hominid migration into Southeast Asia from the one that gave rise to Javan *H. erectus.* Future excavations on Flores and other Indonesian islands (*detail*) may cast light on these mysteries.


HANDOUT/REUTERS/CORBIS (*cave*); LAURIE GRACE AND EDWARD BELL (*maps*)

appear to include few, if any, of the sophisticated types found elsewhere in the cave. This brings up the possibility that the modern-looking tools were produced by modern humans, who could have occupied the cave at a different time. Further excavations are necessary to determine the stratigraphic relation between the implements and the hominid remains, Klein opines. Such efforts may turn up modern humans like us. The question then, he says, will be whether there were two species at the site or whether modern humans alone occupied Liang Bua—in which case LB1 was simply a modern who experienced a growth anomaly.

Stratigraphic concerns aside, the tools are too advanced and too large to make manufacture by a primitive, diminutive hominid likely, Groves contends. Although the Liang Bua implements allegedly date back as far as 94,000 years ago, which the team argues makes them too early to be the handiwork of

*H. sapiens,* Groves points out that 67,000-year-old tools have turned up in Liujiang, China, and older indications of a modern human presence in the Far East might yet emerge. "*H. sapiens,* once it was out of Africa, didn't take long to spread into eastern Asia," he comments.

"At the moment there isn't enough evidence" to establish that *H. floresiensis* created the advanced tools, concurs Bernard Wood of George Washington University. But as a thought experiment, he says, "let's pretend that they did." In that case, "I don't have a clue about brain size and ability," he confesses. If a hominid with no more gray matter than a chimp has can create a material culture like this one, Wood contemplates, "why did it take people such a bloody long time to make tools" in the first place?

"If *Homo floresiensis* was capable of producing sophisticated tools, we have to say that brain size doesn't add up to much," Rightmire concludes. Of course, humans today exhibit considerable variation in gray matter volume, and great thinkers exist at both ends of the spectrum. French writer Jacques Anatole François Thibault (also known as Anatole France), who won the 1921 Nobel Prize for Literature, had a cranial capacity of only about 1,000 cubic centimeters; England's General Oliver Cromwell had more than twice that. "What that means is that once you get the brain to a certain size, size no longer matters, it's the organization of the brain," Potts states. At some point, he adds, "the internal wiring of the brain may allow competence even if the brain seems small."

LB1's brain is long gone, so how it was wired will remain a mystery. Clues to its organization may reside on the interior of the braincase, however. Paleontologists can sometimes obtain latex molds of the insides of fossil skulls and then create plaster endocasts that reveal the morphology of the organ. Because LB1's bones are too fragile to withstand standard casting procedures, Brown is working on creating a virtual endocast based on CT scans of the skull that he can then use to generate a physical endocast via stereolithography, a rapid-prototyping technology.

"If it's a little miniature version of an adult human brain, I'll be really blown away," says paleoneurologist Dean Falk of the University of Florida. Then again, she muses, what happens if the convolutions look chimplike? Specialists have long wondered whether bigger brains fold differently simply because they are bigger or whether the reorganization reflects selection for increased cognition. "This specimen could conceivably answer that," Falk observes.

## Return to the Lost World

SINCE SUBMITTING their technical papers to *Nature,* the Liang Bua excavators have reportedly recovered the remains of another five or so individuals, all of which fit the *H. floresiensis* profile. None are nearly so complete as LB1, whose long arms turned up during the most recent field season. But they did unearth a second lower jaw that they say is identical in size and shape to LB1's. Such duplicate bones will be critical to their case that they have a population of these tiny humans (as opposed to a bunch of scattered bones from one person). That should in turn dispel concerns that LB1 was a diseased individual.

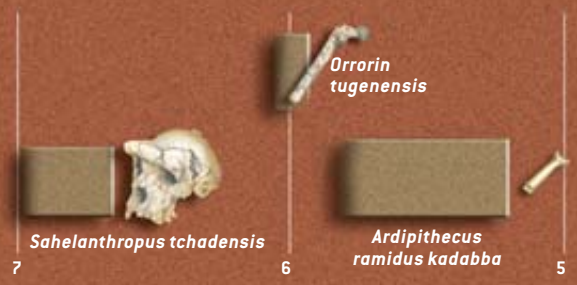
Additional evidence may come from DNA: hair samples possibly from *H. floresiensis* are undergoing analysis at the University of Oxford, and the hominid teeth and bones may contain viable DNA as well. "Tropical environments are not the best for long-term preservation of DNA, so we're not holding our breath," Roberts remarks, "but there's certainly no harm in looking."

The future of the bones (and any DNA they contain) is uncertain, however. In late November, Teuku Jacob of the Gadjah Mada University in Yogyakarta, Java, who was not involved in the discovery or the analyses, had the delicate specimens transported from their repository at the Indonesian Center for Archaeology to his own laboratory with Soejono's assistance. Jacob, the dean of Indonesian paleoanthropology, thinks LB1 was a microcephalic and allegedly ordered the transfer of it and the new, as yet undescribed finds for examination and safekeeping, despite strong objections from other staff members at the center. At the time this article was going to press, the team was waiting for Jacob to make good on his promise to return the remains to Jakarta by January 1 of this year, but his reputation for restricting scientific access to fossils has prompted pundits to predict that the bones will never be studied again.

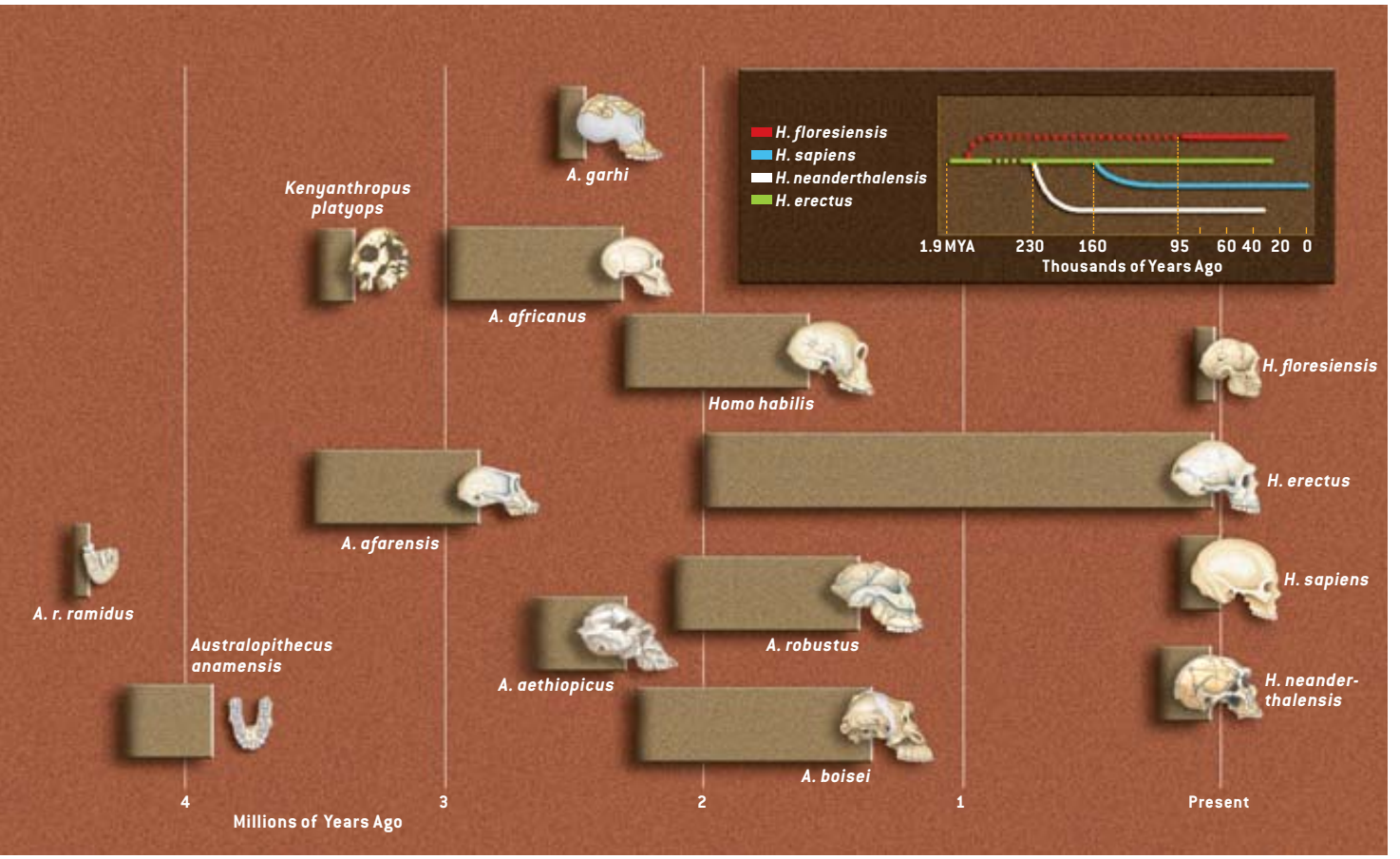
Efforts to piece together the *H. floresiensis* puzzle will proceed, however. For his part, Brown is eager to find the tiny hominid's large-bodied forebears. The possibilities are three-

## The Times of Their Lives

Adding a twig to the family tree of humans, Peter Brown of the University of New England in Armidale, Australia, and his colleagues diagnosed the hominid remains from Flores as a new species of Homo, *H. floresiensis.* This brings the number of hominid forms alive at the time of early *H. sapiens* to four if Neandertals are considered a species separate from our own, as shown here. Brown believes that *H. floresiensis* descended from *H. erectus* (*inset*). Others hypothesize that it is an aberrant *H. sapiens* or *H. erectus* or an offshoot of the earlier and more primitive habilines or australopithecines.




PATRICIA J. WYNNE, CORNELIA BLIK AND EDWARD BELL




fold, he notes. Either the ancestor dwarfed on Flores (and was possibly the maker of the 840,000-year-old Soa Basin tools), or it dwindled on another island and later reached Flores, or the ancestor was small before it even arrived in Southeast Asia. In fact, in many ways, LB1 more closely resembles African *H. erectus* and the Georgian hominids than the geographically closer Javan *H. erectus,* he observes. But whether these similarities indicate that *H. floresiensis* arose from an earlier *H. erectus* foray into Southeast Asia than the one that produced Javan *H. erectus* or are merely coincidental results of the dwarfing process remains to be determined. Future excavations may connect the dots. The team plans to continue digging on Flores and Java and will next year begin work on other Indonesian islands, including Sulawesi to the north.

The hominid bones from Liang Bua now span the period from 95,000 to 13,000 years ago, suggesting to the team that the little Floresians perished along with the pygmy *Stegodon* because of a massive volcanic eruption in the area around 12,000 years ago, although they may have survived later farther east. If *H. erectus* persisted on nearby Java until 25,000 years ago, as some evidence suggests, and *H. sapiens* had arrived in the region by 40,000 years ago, three human species lived cheek by jowl in Southeast Asia for at least 15,000 years. And the discoverers of *H. floresiensis* predict that more will be found. The islands of Lombok and Sumbawa would have been natural stepping-stones for hominids traveling from Java or mainland Asia to Flores. Those that put down roots on these islands may well have set off on their own evolutionary trajectories.

Perhaps, it has been proposed, some of these offshoots of the *Homo* lineage survived until historic times. Maybe they still live in remote pockets of Southeast Asia's dense rain forests, awaiting (or avoiding) discovery. On Flores, oral histories hold that the *ebu gogo* was still in existence when Dutch colonists settled there in the 19th century. And Malay folklore describes another small, humanlike being known as the *orang pendek* that supposedly dwells on Sumatra to this day.

"Every country seems to have myths about these things," Brown reflects. "We've excavated a lot of sites around the world, and we've never found them. But then [in September 2003] we found LB1." Scientists may never know whether tales of the *ebu gogo* and *orang pendek* do in fact recount actual sightings of other hominid species, but the newfound possibility will no doubt spur efforts to find such creatures for generations to come. SA

*Kate Wong is editorial director of ScientificAmerican.com*

## MORE TO EXPLORE

**Archaeology and Age of a New Hominin from Flores in Eastern Indonesia.** M. J. Morwood et al. in *Nature,* Vol. 431, pages 1087–1091; October 28, 2004.

**A New Small-Bodied Hominin from the Late Pleistocene of Flores, Indonesia.** P. Brown et al. in *Nature,* Vol. 431, pages 1055–1061; October 28, 2004.

A Q&A with Peter Brown is at **www.sciam.com/ontheweb**


BARRAGE of Internet information will drop to a focused trickle with new search engines that can take context—such as a user's long-term interests, location or other factors—into account.

By Javed Mostafa

Illustrations by Neil Brennan

# Seeking Better Web Searches

## Deluged with superfluous responses to online queries, users will soon benefit from improved search engines that deliver customized results

In less than a decade, Internet search engines have completely changed how people gather information. No longer must we run to a library to look up something; rather we can pull up relevant documents with just a few clicks on a keyboard. Now that "Googling" has become synonymous with doing research, online search engines are poised for a series of upgrades that promise to further enhance how we find what we need.

New search engines are improving the quality of results by delving deeper into the storehouse of materials available online, by sorting and presenting those results better, and by tracking your long-term interests so that they can refine their handling of new information requests. In the future, search engines will broaden content horizons as well, doing more than simply processing keyword queries typed into a text box. They will be able to automatically take into account your location—letting your wireless PDA, for instance, pinpoint the nearest restaurant when you are traveling. New systems will also find just the right picture faster by matching your sketches to similar shapes. They will even be able to name that half-remembered tune if you hum a few bars.

Today's search engines have their roots in a research field called information retrieval, a computing topic tracing back nearly 50 years. In a September 1966 *Scientific American* article, "Information Storage and Retrieval," Ben Ami Lipetz described how the most advanced information technologies of the day could han-

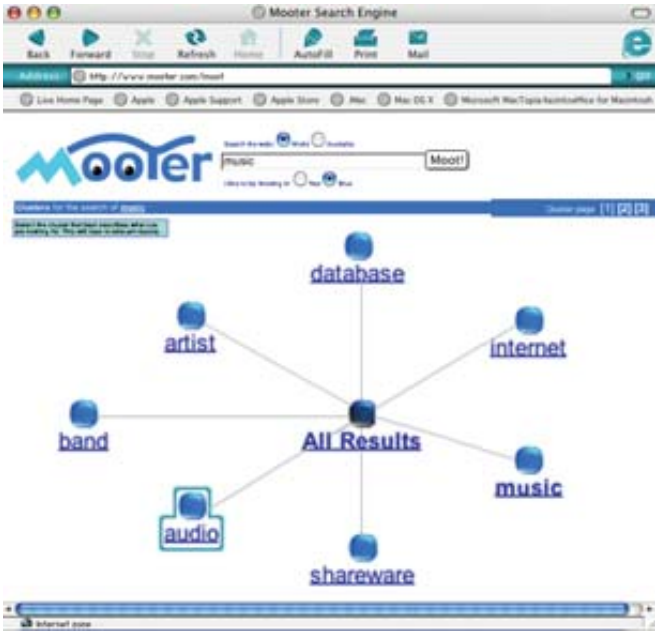
dle only routine or clerical tasks. He then concluded perceptively that breakthroughs in information retrieval would come when researchers gained a deeper understanding of how humans process information and then endowed machines with analogous capabilities. Clearly, computers have not yet reached that level of sophistication, but they are certainly taking users' personal interests, habits and needs into greater account when completing tasks.

## Prescreened Pages

BEFORE DISCUSSING new developments in this field, it helps to review how current search engines operate. What happens when a computer user reads on a screen that Google has sifted through billions of documents in, say, 0.32 second? Because matching a user's keyword query with a single Web page at a time would take too long, the systems carry out several key steps long before a user conducts a search.

First, prospective content is identified and collected on an ongoing basis. Special software code called a crawler is used to probe pages published on the Web, retrieve these and linked pages, and aggregate pages in a single location. In the second step, the system counts relevant words and establishes their importance using various statistical techniques. Third, a highly efficient data structure, or tree, is generated from the relevant terms, which associates those terms with specific Web pages. When a user submits a query, it is the completed tree, also known as an index, that is searched and not individual Web pages. The search starts at the root of the index tree, and at every step a branch of the tree (representing many terms and related Web pages) is either followed or eliminated from consideration, reducing the time to search in an exponential fashion.

To place relevant records (or links) at or near the top of the retrieved list, the search algorithm applies various ranking strategies. A common ranking method—term frequency/inverse document frequency—considers the distribution of words and their frequencies, then generates numerical weights for words that signify their importance in individual documents. Words that are frequent (such as "or," "to" or "with") or that appear in many documents are given substantially less weight than words that are more relevant semantically or appear in comparatively few documents.




MOOTER, a new search engine, simplifies the user's assessment of results by categorizing the collected information and clustering related sites under on-screen buttons. Subcategory buttons surround the central general topic cluster. Clicking on a cluster button retrieves lists and new, associated clusters.

In addition to term weighting, Web pages can be ranked using other strategies. Link analysis, for example, considers the nature of each page in terms of its association with other pages—namely, if it is an authority (by the number of other pages that point to it) or a hub (by the number of pages it points to). Google uses link analysis to improve the ranking of its search results.

## Superior Engines

DURING THE SIX YEARS in which Google rose to dominance, it offered two critical advantages over competitors. One, it could handle extremely large-scale Web crawling tasks. Two, its indexing and weighting methods produced superior ranking results. Recently, however, search engine builders have developed several new, similarly capable schemes, some of which are even better in certain ways.

Much of the digital content today remains inaccessible because many systems hosting (holding and handling) that material do not store Web pages as users normally view them. These resources generate Web pages on demand as users interact with them. Typical crawlers are stumped by these resources and fail to retrieve any content. This keeps a huge amount of information—approximately 500 times the size of the conventional Web, according to some estimates—concealed from users. Efforts are under way to make it as easy to search the "hidden Web" as the visible one.

To this end, programmers have developed a class of soft-

## Overview/*Beyond Google*

- As Web sites continue to multiply rapidly, Internet users need more precise search engines that find what they are looking for more quickly and efficiently.
- The next search engines will improve results by digging deeper through online materials, by better classifying and displaying the catch, and by monitoring users' interests to respond more intelligently to future searches. New software will track a user's location and will handle graphics and music as well as text.
- New business models will eventually open up nearly all published digital information—text, audio and video resources that are currently unavailable on the Web—to smart search functions.

WWW.MOOTER.COM

Efforts are under way to make it as easy to

## search the "hidden Web" as the visible one.

ware, referred to as wrappers, that takes advantage of the fact that online information tends to be presented using standardized "grammatical" structures. Wrappers accomplish their task in various ways. Some exploit the customary syntax of search queries and the standard formats of online resources to gain access to hidden content. Other systems take advantage of application programming interfaces, which enable software to interact via a standard set of operations and commands. An example of a program that provides access to the hidden Web is Deep Query Manager from BrightPlanet. This wrapper-based query manager can provide customized portals and search interfaces to more than 70,000 hidden Web resources.

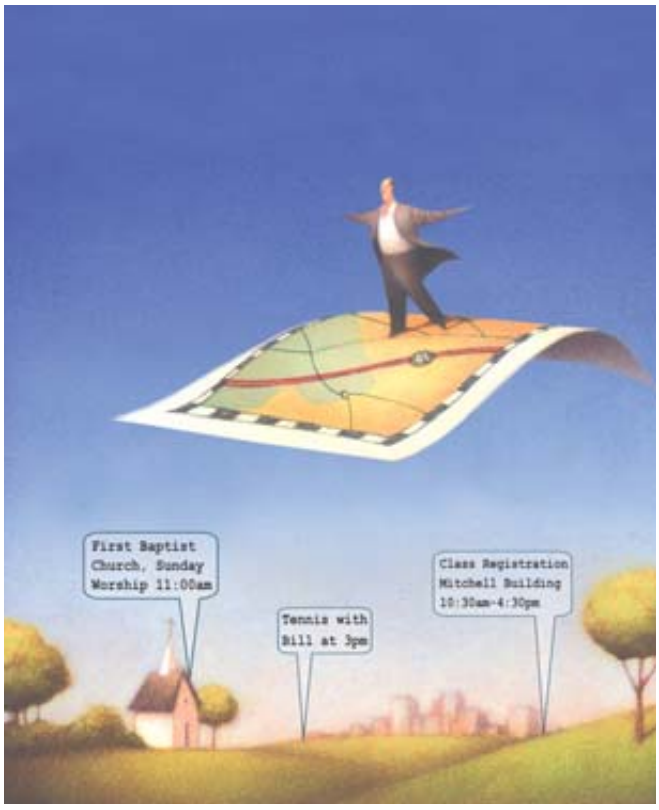
Relying solely on links or words to establish ranking, without placing any constraint on the types of pages that are being compared, opens up possibilities for spoofing or gaming the ranking system to misdirect queries. When the query "miserable failure," for example, is executed on the three top search engines—Google, Yahoo and MSN—a page from the whitehouse.gov site appears as the top item in the resulting set of retrieved links.

Rather than providing the user with a list of ranked items (which can be spoofed relatively easily), certain search engines attempt to identify patterns among those pages that most closely match the query and group the results into smaller sets. These patterns may include common words, synonyms, related words or even high-level conceptual themes that are identified using special rules. These systems label each set of links with its relevant term. A user can then refine a search further by selecting a particular set of results. Northern Light (which pioneered this technique) and Clusty are search engines that present clustered results.

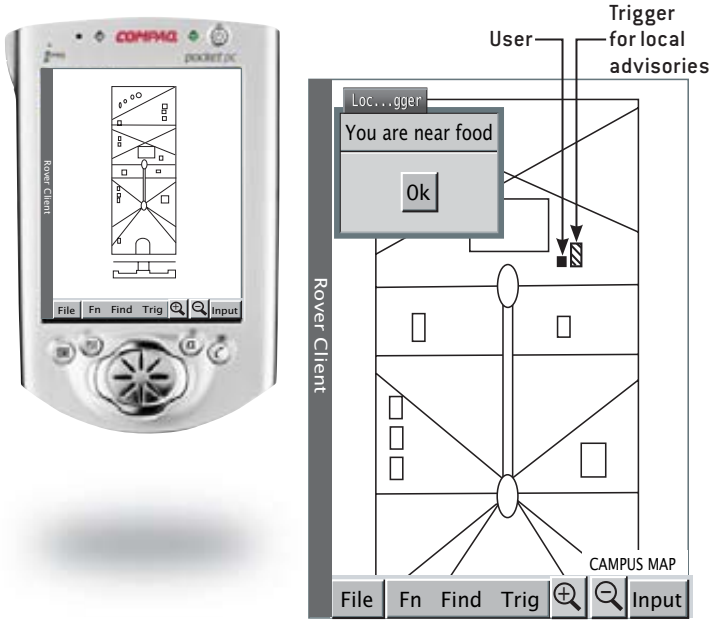
Mooter, an innovative search engine that also employs clustering techniques, provides researchers with several additional advantages by presenting its clusters visually [*see illustration on opposite page*]. It arrays the subcategory buttons around a central button representing all the results, like the spokes of a wheel. Clicking on a cluster button retrieves lists of relevant links and new, associated clusters. Mooter remembers the chosen clusters. By clicking on the "refine" option, which combines previously retrieved search clusters with the current query, a user can obtain even more precise results.

A similar search engine that also employs visualization is Kartoo. It is a so-called metasearch engine that submits the user's query to other search engines and provides aggregated results in a visual form. Along with a list of key terms associated with various sites, Kartoo displays a "map" that depicts important sites as icons and relations among the sites as labeled paths. Each label can be used to further refine the search.

Another way computer tools will simplify searches is by looking through your hard drive as well as the Web. Currently




I KNOW WHERE WE ARE: A computing environment that is aware of its location, such as the University of Maryland's Rover technology, makes it possible for a wireless handheld device to know its position on the map at all times. This feature allows Rover to provide customized information about the local surroundings to the user on the go.




MIND LAB, UNIVERSITY OF MARYLAND, COLLEGE PARK

Recently Amazon, Ask Jeeves and Google announced initiatives that would **allow users to personalize their searches.**

searches for a file on a computer user's desktop require a separate software application. Google, for example, recently announced Desktop Search, which combines the two functions, allowing a user to specify a hard disk or the Web, or both, for a given search. The next release of Microsoft's operating system, code-named Longhorn, is expected to supply similar capabilities. Using techniques developed in another Microsoft project called Stuff I've Seen, Longhorn may offer "implicit search" capabilities that can retrieve relevant information without the user having to specify queries. The implicit search feature reportedly harvests keywords from textual information recently manipulated by the user, such as e-mail or Word documents, to locate and present related content from files stored on a user's hard drive. Microsoft may extend the search function to Web content and enable users to transform any text content displayed on screens into queries more conveniently.

## Search Me

RECENTLY AMAZON, Ask Jeeves and Google announced initiatives that attempt to improve search results by allowing users to personalize their searches. The Amazon search engine, A9.com, and the Ask Jeeves search engine, MyJeeves.ask.com, can track both queries and retrieved pages as well as allow users to save them permanently in bookmark fashion. In MyJeeves, saved searches can be reviewed and reexecuted, providing a way to develop a personally organized subset of the Web. Amazon's A9 can support similar functions and also employs personal search histories to suggest additional pages. This advisory function resembles Amazon's well-known book recommendation feature, which takes advantage of search and purchasing patterns of communities of users—a process sometimes called collaborative filtering.

The search histories in both A9 and MyJeeves are saved not on users' machines but on search engine servers so that they can be secured and later retrieved on any machine that is used for subsequent searches.

In personalized Google, users can specify subjects that are of particular interest to them by selecting from a pregenerated hierarchy of topics. It also lets users specify the degree to which they are interested in various themes or fields. The system then employs the chosen topics, the indicated level of interest, and the original query to retrieve and rank results.

Although these search systems offer significant new features, they represent only incremental enhancements. If search engines could take the broader task context of a person's query into account—that is, a user's recent search subjects, personal behavior, work topics, and so forth—their utility would be greatly augmented. Determining user context will require software designers to surmount serious engineering hurdles, however. Developers must first build systems that monitor a user's interests and habits automatically so that search engines can ascertain the context in which a person is conducting a search for information, the type of computing platform a user is running, and his or her general pattern of use. With these points established beforehand and placed in what is called a user profile, the software could then deliver appropriately customized information. Acquiring and maintaining accurate information about users may prove difficult. After all, most people are unlikely to put up with the bother of entering personal data other than that required for their standard search activities.

Good sources of information on personal interests are the records of a user's Web browsing behavior and other interactions with common applications in their systems. As a person opens, reads, plays, views, prints or shares documents, engines could track his or her activities and employ them to guide searches of particular subjects. This process resembles the implicit search function developed by Microsoft. PowerScout and Watson are the first systems introduced capable of integrating searches with user-interest profiles generated from indirect sources. PowerScout has remained an unreleased laboratory system, but Watson seems to be nearing commercialization. Programmers are now developing more sophisticated software that will collect interaction data over time and then generate and maintain a user profile to predict future interests.

The user-profile-based techniques in these systems have not been widely adopted, however. Various factors may be responsible: one issue may be the problems associated with maintaining profile accuracy across different tasks and over extended periods. Repeated evaluation is necessary to establish robust profiles. A user's focus can change in unpredictable and subtle ways, which can affect retrieval results dramatically.

Another factor is privacy protection. Trails of Web navigation, saved searches and patterns of interactions with applications can reveal a significant amount of secret personal information (even to the point of revealing a user's identity). A handful of available software systems permit a user to obtain content from Web sites anonymously. The primary means used by these tools are intermediate or proxy servers through which a user's transactions are transmitted and processed so that the site hosting the data or service is only aware of the proxy systems and cannot trace a request back to an individual user. One instance of this technology is the anonymizer.com site, which permits a user to browse the Web incognito. An addi-

THE AUTHOR

*JAVED MOSTAFA* is Victor H. Yngve Associate Professor of Information Science at Indiana University. He is an associate editor of *ACM Transactions on Information Systems* and directs the Laboratory of Applied Informatics Research at Indiana. The author dedicates this article to one of his favorite teachers, Ms. Shaila of BWA School in Chittagong, Bangladesh.

tional example is the Freedom WebSecure software, which employs multiple proxies and many layers of encryption. Although these tools offer reasonable security, search services do not yet exist that enable both user personalization and strong privacy protection. Balancing the maintenance of privacy with the benefits of profiles remains a crucial challenge.

## On the Road

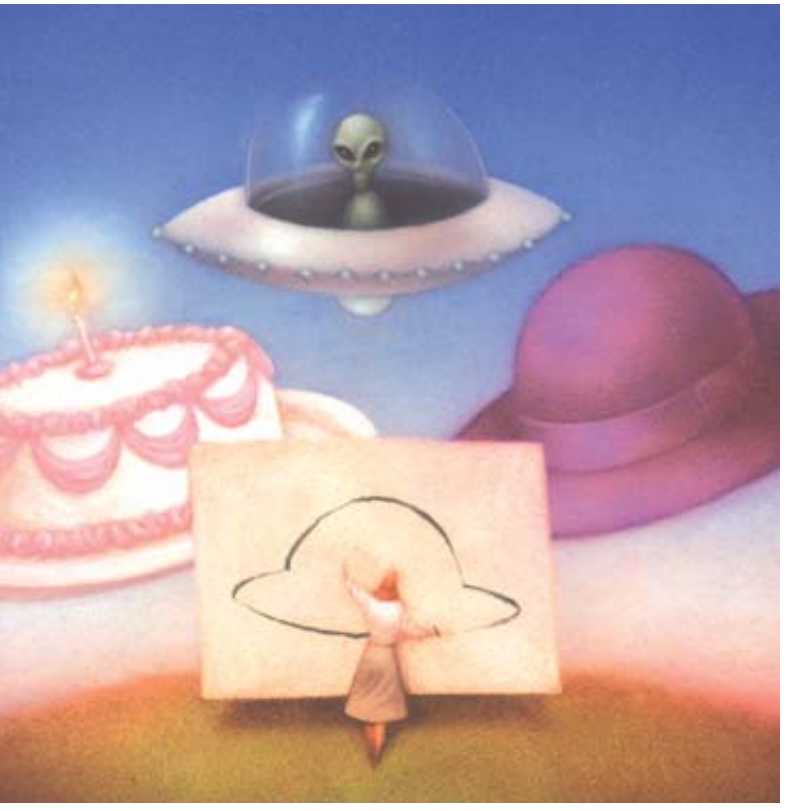
ANOTHER CLASS of context-aware search systems would take into account a person's location. If a vacationer, for example, is carrying a PDA that can receive and interpret signals from the Global Positioning System (GPS) or using a radio-frequency technique to establish and continuously update position, systems could take advantage of that capability. One example of such a technology is being developed by researchers at the University of Maryland. Called Rover, it is a system that makes use of text, audio or video services across a wide geographic area [*see illustration on page 69*]. Rover can present maps of the region in a user's vicinity that highlight appropriate points of interest. It is able to identify these spots automatically by applying various subject-specific "filters" to the map.

The system can provide additional information as well. If a Rover client were visiting a museum, for example, the handheld device would show the institution's floor plan and nearby displays. If the user stepped outside, the PDA display would change to an area map marking locations of potential interest. Rover would also permit an operator to enter his or her position directly and retrieve customized information from the networked database. In 2003 the group that created Rover and KoolSpan, a private network company, received funding from the Maryland state government to develop jointly applications for secure wireless data delivery and user authentication. This collaboration should result in a more secure and commercially acceptable version of Rover.

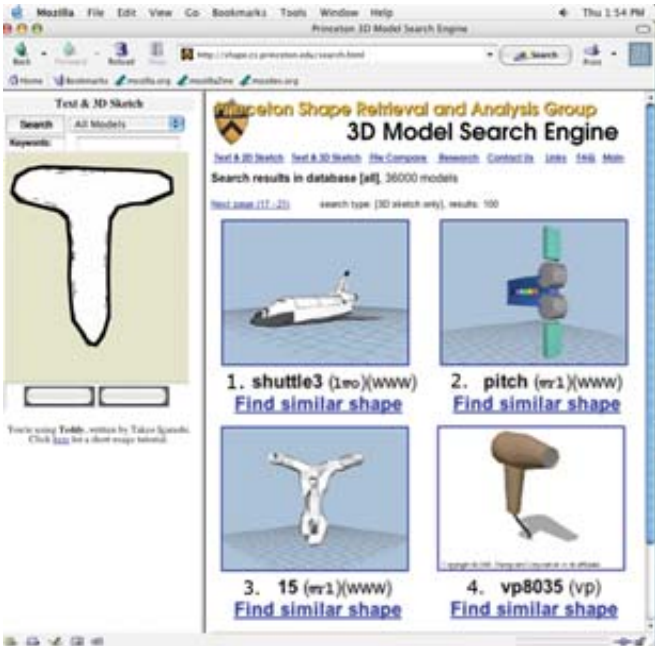
Unfortunately, the positional error of GPS-based systems (from three to four meters) is still rather large. Even though this resolution can be enhanced by indoor sensor and outdoor beacon systems, these technologies are relatively expensive to implement. Further, the distribution of nontext information, especially images, audio and video, would require higher bandwidth capacities than those currently available from handheld devices or provided by today's wireless networks. The IEEE 802.11b wireless local-area network protocol, which offers bandwidths of up to 11 megabits per second, has been tested successfully in providing location-aware search services but is not yet widely available.

## Picture This

CONTEXT CAN MEAN MORE than just a user's personal interests or location. Search engines are also going beyond text queries to find graphical material. Many three-dimensional images are now available on the Web, but artists, illustrators and designers cannot effectively search through these drawings or shapes using keywords. The Princeton Shape Retrieval and Analysis Group's 3-D Model Search Engine supports three methods to generate such a query [*see illustration below*]. The first approach uses a sketchpad utility called Teddy, which allows a person to draw basic two-dimensional shapes. The soft-



THOMAS FUNKHOUSER, PRINCETON SHAPE RETRIEVAL AND ANALYSIS GROUP




FIND THAT SHAPE: The 3-D Model Search Engine from the Princeton Shape Retrieval and Analysis Group matches a desired shape with multiple images of similar forms available on the Internet. Designers, engineers and architects can locate analogous three-dimensional objects much more rapidly than before.

**Web searchers will steer through voluminous data repositories using interfaces that establish broad patterns in information.**

ware then produces a virtual solid extrusion (by dragging 2-D images through space) from those shapes. The second lets a user draw multiple two-dimensional shapes (approximating different projections of an image), and the search engine then matches the flat sketches to 13 precomputed projections of each three-dimensional object in its database. Theoretically, this function can be generalized to support retrieval from any 2-D image data set. The third way a person can find an image is to upload a file containing a three-dimensional model.

The system, still in development, matches queries to shapes by first describing each shape in terms of a series of mathematical functions—harmonic functions for three-dimensional images and trigonometric ones for two-dimensional representations. The system then produces certain "fingerprinting" values from each function that are characteristic for each associated shape. These fingerprints are called spherical or circular signatures. Two benefits arise from using these descriptors: they can be matched no matter how the original and search shapes are oriented, and the descriptors may be computed and matched rapidly.

## What's That Song?

MUSIC HAS ALSO ENTERED the search engine landscape. A key problem in finding a specific tune is how to best formulate the search query. One type of solution is to use musical notation or a musical transcription-based query language that permits a user to specify a tune by keying in alphanumeric characters to represent musical notes. Most users, however, find it difficult to transform the song they have in mind to musical notation.

The Meldex system, designed by the New Zealand Digital Library Project, solves the problem by offering a couple of ways to find music [*see illustration on opposite page*]. First, a user can record a query by playing notes on the system's virtual keyboard. Or he or she can hum the song into a computer microphone. Last, users can specify song lyrics as a text query or combine a lyrics search with a tune-based search.

To make the Meldex system work, the New Zealand researchers had to overcome several obstacles: how to convert the musical query to a form that could be readily computed; how to store and search song scores digitally; and how to match those queries with the stored musical data. In the system, a process called quantization identifies the notes and pitches in a query. Meldex then detects the pitches as a function of time automatically by analyzing the structure of the waveforms and maps them to digital notes. The system stores both notes and complete works in a database of musical scores. Using data string-matching algorithms, Meldex finds musical queries converted into notes that correspond with notes from the scores database. Because the queries may contain errors, the string-matching function must accommodate a certain amount of "noise."

## Searching the Future

FUTURE SEARCH SERVICES will not be restricted to conventional computing platforms. Engineers have already integrated them into some automotive mobile data communications (telematics) systems, and it is likely they will also embed

## PLACING ALL MEDIA ON THE NET

Although the Internet covers a tremendous amount of information, much of what is published today—text, audio and video—is not available online. Content is costly, and its producers want to exercise maximum control over what they generate, so they limit access severely. That situation is changing, however, as collaboration grows among content producers (such as Time-Warner, Sony, Hearst, Elsevier, and so forth) and "brand-name" search engine players (particularly the big three, Yahoo, Google and MSN). The challenge is to forge business relations that are beneficial to both sides.

If suitable contractual agreements were established between media publishers and search engine companies, arranging for the content producers' sites to be crawled and indexed by search engines would be relatively straightforward. Say a search engine user were to find a citation to a specific content producer's item; the link could then route the user to the appropriate site for access. There the user could be offered various options for obtaining the complete content.

In some pilot projects, content providers are allowing indexing of their raw product. Amazon, for instance, has instituted an experimental project through which customers can read the full texts of books. Google recently introduced a service for publishers and large libraries to submit their books for indexing so they can be included in the same indexes as Web content.

Related concerns exist in the audio and video fields. Production houses and studios are reluctant to adopt new avenues of distribution. Here, too, however, alternative marketing models are appearing. Apple has promoted its iTunes music store aggressively, and both Dell and Hewlett-Packard have announced music delivery services.

Eventually, industry observers say, search engines will most likely serve as "hubs" or gateways to all types of content. They will generate and maintain indexes as well as provide search services for diverse classes of published media. Content providers will meanwhile concentrate on their core creative businesses. —*J.M.*

NAME THAT TUNE: Formulating a query to find a particular song or melody in an Internet-based musical database is not easy for people without formal music training. The Meldex system from the New Zealand Digital Library Project lets a user hum a half-remembered tune into a PC's microphone or type in some of its lyrics, and the software identifies the matching song or melody fast.


search capabilities into entertainment equipment such as game stations, televisions and high-end stereo systems. Thus, search technologies will play unseen ancillary roles, often via intelligent Web services, in activities such as driving vehicles, listening to music and designing products.

Another big change in Web searching will revolve around new business deals that greatly expand the online coverage of the huge amount of published materials, including text, video and audio, that computer users cannot currently access [*see box on opposite page*].

Ironically, next-generation search technologies will become both more and less visible as they perform their increasingly sophisticated jobs. The visible role will be represented by more powerful tools that combine search functions with data-mining operations—specialized systems that look for trends or anomalies in databases without actually knowing the meaning of the data. The unseen role will involve developing myriad intelligent search operations as back-end services for diverse applications and platforms. Advances in both data-mining and user-interface technologies will make it possible for a single system to provide a continuum of sophisticated search services automatically that are integrated seamlessly with interactive visual functions.

By leveraging advances in machine learning and classification techniques that will be able to better understand and categorize Web content, programmers will develop easy-to-use visual mining functions that will add a highly visible and interactive dimension to the search function. Industry analysts expect that a variety of mining capabilities will be available, each tuned to search content from a specialized domain or format (say, music or biological data). Software engineers will design these functions to respond to users' needs quickly and conveniently despite the fact they will manipulate vast quantities of information. Web searchers will steer through voluminous data repositories using visually rich interfaces that focus on establishing broad patterns in information rather than picking out individual records. Eventually it will be difficult for computer users to determine where searching starts and understanding begins. SA

## MORE TO EXPLORE


**Information Storage and Retrieval.** Ben Ami Lipetz in *Scientific American*, Vol. 215, No. 3, pages 224–242; September 1966.

**Exploring the Web with Reconnaissance Agents.** H. Lieberman, C. Fry and L. Weitzman in *Communications of the ACM*, Vol. 44, No. 8, pages 69–75; August 2001.

**Web Search—Your Way.** E. Glover et al. in *Communications of the ACM*, Vol. 44, No. 12, pages 97–102; December 2001.

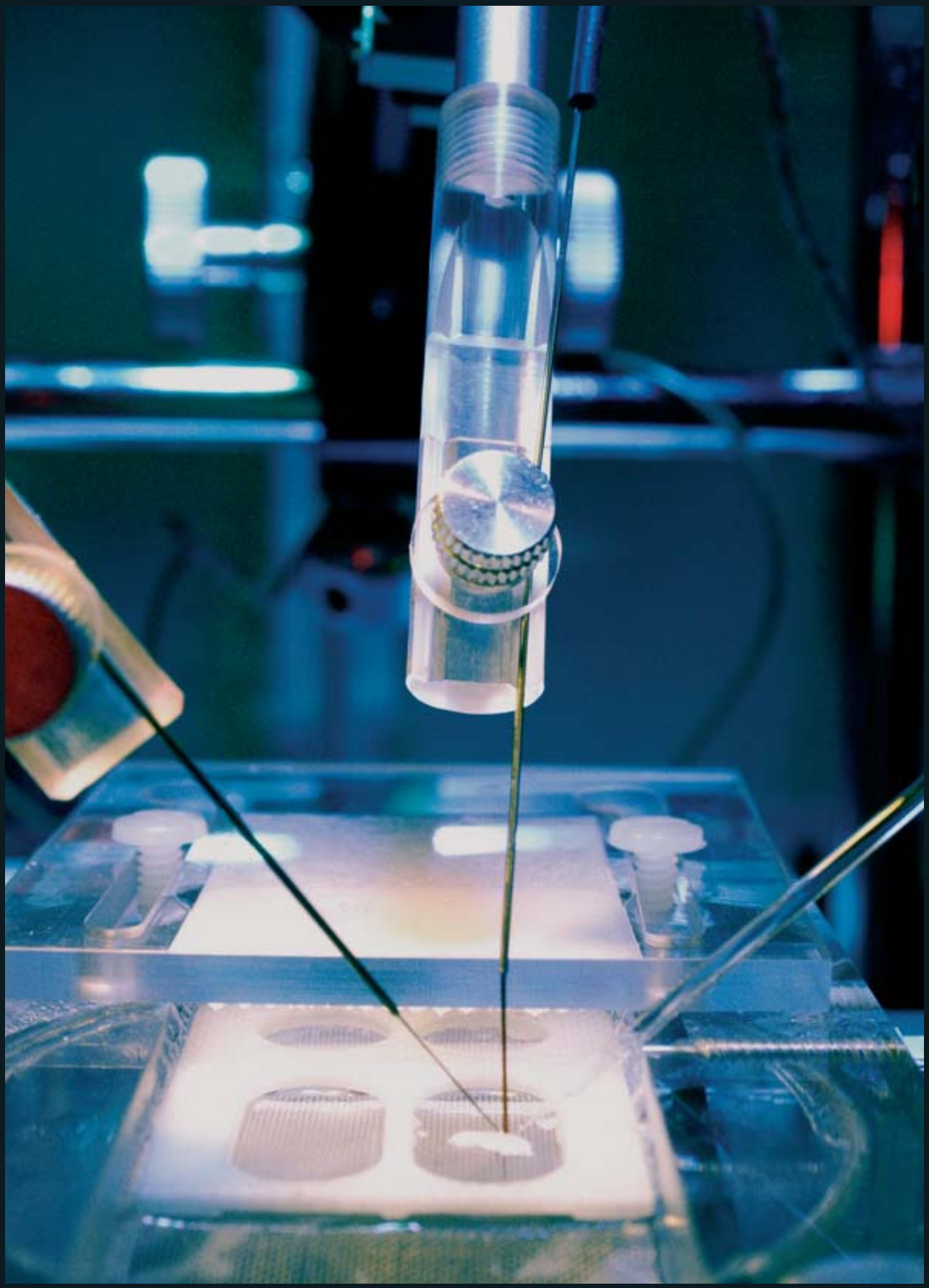
**Rover: Scalable Location-Aware Computing.** S. Banerjee et al. in *Computer*, Vol. 35, No. 10, pages 46–53; October 2002.

**A Search Engine for 3D Models.** T. Funkhouser et al. in *ACM Transactions on Graphics*, Vol. 22, No. 1, pages 83–105; January 2003.

**Simulation Studies of Different Dimensions of Users' Interests and Their Impact on User Modeling and Information Filtering.** Javed Mostafa, S. Mukhopadhyay and M. Palakal in *Information Retrieval*, Vol. 6, No. 2, pages 199–223; April 2003.


For the URLs of the Web sites referred to in the article, see **www.sciam.com/ontheweb**

NEW ZEALAND DIGITAL LIBRARY PROJECT, UNIVERSITY OF WAIKATO



TO SIMULATE MEMORY FORMATION, an electrophysiological recording apparatus can both stimulate and record electrical signals from a 400-micron-thick slice of rat hippocampus.

KAY CHERNUSH

# MAKING MEMORIES STICK

**Some moments become lasting recollections while others just evaporate. The reason may involve the same processes that shape our brains to begin with**

BY R. DOUGLAS FIELDS

In the movie thriller *Memento*, the principal character, Leonard, can remember everything that happened before his head injury on the night his wife was attacked, but anyone he meets or anything he has done since that fateful night simply vanishes. He has lost the ability to convert short-term memory into long-term memory. Leonard is driven to find his wife's killer and avenge her death, but trapped permanently in the present, he must resort to tattooing the clues of his investigation all over his body.

That disturbing story was inspired by the real case history of a patient known in the medical literature only as "HM." When HM was nine years old, a head injury in a bicycle accident left him with debilitating epilepsy. To relieve his seizures that could not be controlled in any other way, surgeons removed parts of HM's hippocampus and adjoining brain regions. The operation succeeded in reducing the brain seizures but inadvertently severed the mysterious link between short-term and long-term memory. Information destined for what is known as declarative memory—people, places, events—must pass through the hippocampus before being recorded in the cerebral cortex. Thus, memories from long ago that were already stored in HM's brain remained clear, but all his experiences of the present soon faded into nothing. HM saw his doctor on a monthly basis, but at each visit it was as if the two had never met.

This transition from the present mental experience to an enduring memory has long fascinated neuroscientists. A person's name when you are first introduced is stored in short-term memory and may be gone within a few minutes. But some information, like your best friend's name, is converted into long-term memory and can persist a lifetime. The mechanism by which the brain preserves certain moments and allows others to fade has recently become clearer, but first neuroscientists had to resolve a central paradox.

Both long- and short-term memories arise from the connections between neurons, at points of contact called synapses, where one neuron's signal-emitting extension, called

an axon, meets any of an adjacent neuron's dozens of signal-receiving fingers, called dendrites [*see box on opposite page*]. When a short-term memory is created, stimulation of the synapse is enough to temporarily "strengthen," or sensitize, it to subsequent signals. For a long-term memory, the synapse strengthening becomes permanent. Scientists have been aware since the 1960s, however, that this requires genes in the neuron's nucleus to activate, initiating the production of proteins.

Memory researchers have puzzled over how gene activity deep in the cell nucleus could govern activities at faraway synapses. How does a gene "know" when to strengthen a synapse permanently and when to let a fleeting moment fade unrecorded? And how do the proteins encoded by the gene "know" which of thousands of synapses to strengthen? The same questions have implications for understanding fetal brain development, a time when the brain is deciding which synaptic connections to keep and which to discard. In studying that phenomenon, my lab came up with an intriguing solution to one of these mysteries of memory. And just like Dorothy, we realized that the answer was there all the time.

## HOW DOES A GENE "KNOW" WHEN TO STRENGTHEN A SYNAPSE PERMANENTLY?

### Genetic Memory

EARLY MOLECULAR BIOLOGISTS discovered that genes play a role in the conversion of a memory from short- to long-term. Their experiments with animals trained to perform simple tasks demonstrated that learning required new proteins to be synthesized in the brain within minutes of training, or else the memory would be lost [see "Memory and Protein Synthesis," by Bernard W. Agranoff; SCIENTIFIC AMERICAN, June 1967].

For a protein to be produced, a stretch of DNA inside the cell nucleus must be transcribed into a portable form called messenger RNA (mRNA), which then travels out to the cell's cytoplasm, where cellular machinery translates its encoded instructions into a protein. These researchers had found that blocking the transcription of DNA into mRNA or the translation of mRNA into a protein would impede long-term memory formation but that short-term memory was unaffected.

Because one neuron can form tens of thousands of synaptic connections and there could not possibly be a gene dedicated to each one, cellular neuroscientists sought to explain how the cell nucleus was controlling the strength of these individual connections. They theorized that an unknown signaling molecule must be generated by a synapse when it was sufficiently stimulated. With its connection temporarily strengthened, this synapse could hold the memory for a short time while the signaling molecule departed, wending its way to the nucleus of the nerve cell. There this messenger molecule would activate appropriate genes needed to synthesize proteins that would permanently strengthen the synaptic connection. Yet a second problem was how this protein, once it was manufactured in the cell body of the neuron, could then find the one synapse among thousands that had called for it.

By the mid-1990s, memory researchers had a more detailed picture of events [*see box on page 78*]. Several of them had shown that a transcription factor named CREB played a key role in converting short-term memory into long-term memory in animals as distantly related as flies and mice. Transcription factors are master proteins inside the cell nucleus that find and bind to specific sequences of DNA. They are thus the ultimate on/off switches that control a gene's transcription. So CREB activation within a neuron leads to gene activation, leading to manufacture of the mysterious synapse-strengthening proteins that transform a short-term memory into a long-term one.

In 1997 elegant experiments by Uwe Frey of the German Federal Institute for Neurobiology, Gene Regulation and Plasticity and Richard G. M. Morris of the University of Edinburgh further showed that whatever these "memory proteins" were, they did not need to be addressed to a particular synapse. They could be broadcast throughout the cell but would only affect the synapse that was already temporarily strengthened and make that connection permanently stronger.

These revelations still left at least one more burning question: What is the synapse-to-nucleus signaling molecule that determines when CREB should be activated and a memory preserved? Around this time, my colleagues and I found ourselves approaching the same problems as the memory researchers from a different perspective. In my laboratory at the National Institute of Child Health and Human Development, we study how the brain becomes wired up during fetal devel-

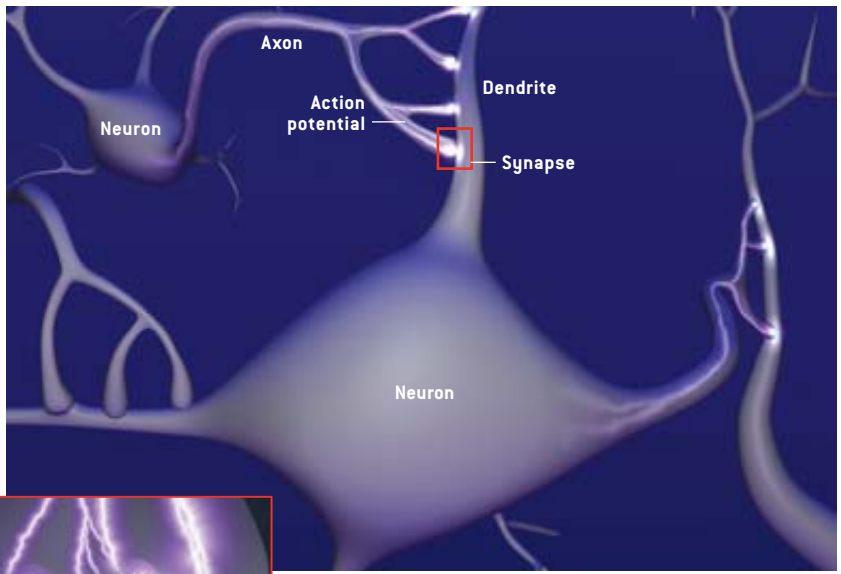
## Overview/*Hardwiring Memory*

- Individual nerve cells somehow know which memories to preserve in the form of lasting connections to other nerve cells and which to let fade. Similarly, the developing brain somehow chooses certain neural circuits to preserve and others to discard.
- Both processes require electrochemical signals from the far edges of a nerve cell to activate genes in the cell nucleus and the genes to direct an answer back to the cell's extremity.
- Like many of life's decisions, the neuron's choice to cement a connection comes only after its importance has been demonstrated.

## MAKING MEMORIES

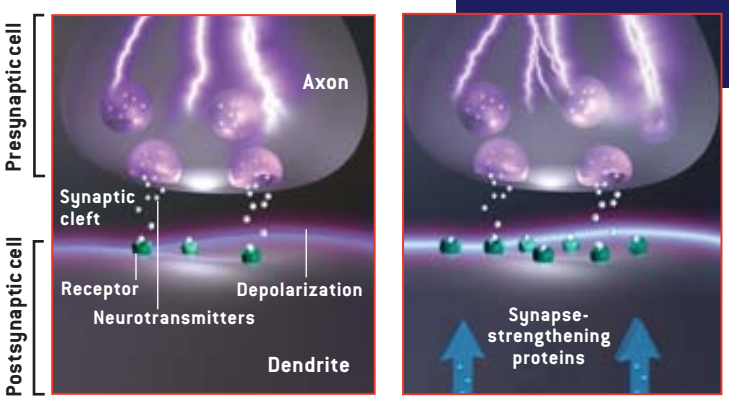
Memories are created when nerve cells in a circuit increase the strength of their connections, known as synapses. In the case of short-term memories, the effect lasts only minutes to hours. For long-term memories, the synapses become permanently strengthened.

Signaling itself contributes to memory formation. Messages begin to travel between one neuron (the presynaptic cell) and another when an electrical pulse known as an action potential (*below*) travels down an extension of the first neuron called an axon to its tip.




### SIGNALING AT THE SYNAPSE

At the axon terminal (*inset below*), the pulse causes synaptic vesicles in the presynaptic neuron to release chemicals called neurotransmitters into a gap, or synaptic cleft, between the axon and a dendrite on the second, postsynaptic neuron. The neurotransmitters bind to receptors on the dendrite, triggering a local depolarization of the postsynaptic cell's membrane that is described as a "firing" of the synapse.




### SYNAPSE STRENGTHENING

After a synapse fires briefly at high frequency, it becomes more sensitive, experiencing a greater voltage swing in response to subsequent signals. This temporary strengthening of the synapse is the basis of short-term memory. Although the process is poorly understood, investigators know that permanent strengthening to form long-term memories requires the postsynaptic cell to manufacture synapse-strengthening proteins (*left*). These proteins might add more receptors and otherwise remodel the postsynaptic part of the synapse as well as possibly influence the presynaptic cell's responses.

opment. So while memory researchers were wondering how mental experience could affect genes, which could in turn affect certain synaptic connections, we were wondering how genes could specify all the millions of connections in the developing brain in the first place.

We and other developmental neuroscientists already suspected that mental experience might have some role in honing the brain's wiring plan. The fetal brain could start out with a rough neural circuitry that was specified by genetic instructions. Then, as the young brain developed and tested those connections, it would preserve the most effective ones and eliminate the poor ones. But how, we wondered, does the brain identify which connections are worth keeping?

## Building a Brain

AS FAR BACK AS 1949, a psychologist named Donald Hebb proposed a simple rule that could govern how experience might bolster certain neural circuits. Inspired by the famous Pavlovian dog experiments, Hebb theorized that connections among neurons that fired at the same time should become strengthened. For example, a neuron that fired when a bell sounded and a nearby neuron that fired when food was presented simultaneously should become more strongly connected to each other, forming a cellular circuit that learns that the two events are connected.

Not every input to a nerve cell is strong enough to make that cell fire a signal of its own. A neuron is like a microprocessor chip in that it receives thousands of signals through its dendrites and constantly integrates all the input it receives from these connections. But unlike a microprocessor that has many output wires, a neuron has only one, its axon. Thus, a neuron can respond to inputs in only one way: it can either decide to send a signal on to the next neuron in the circuit by firing an impulse through its axon, or not.

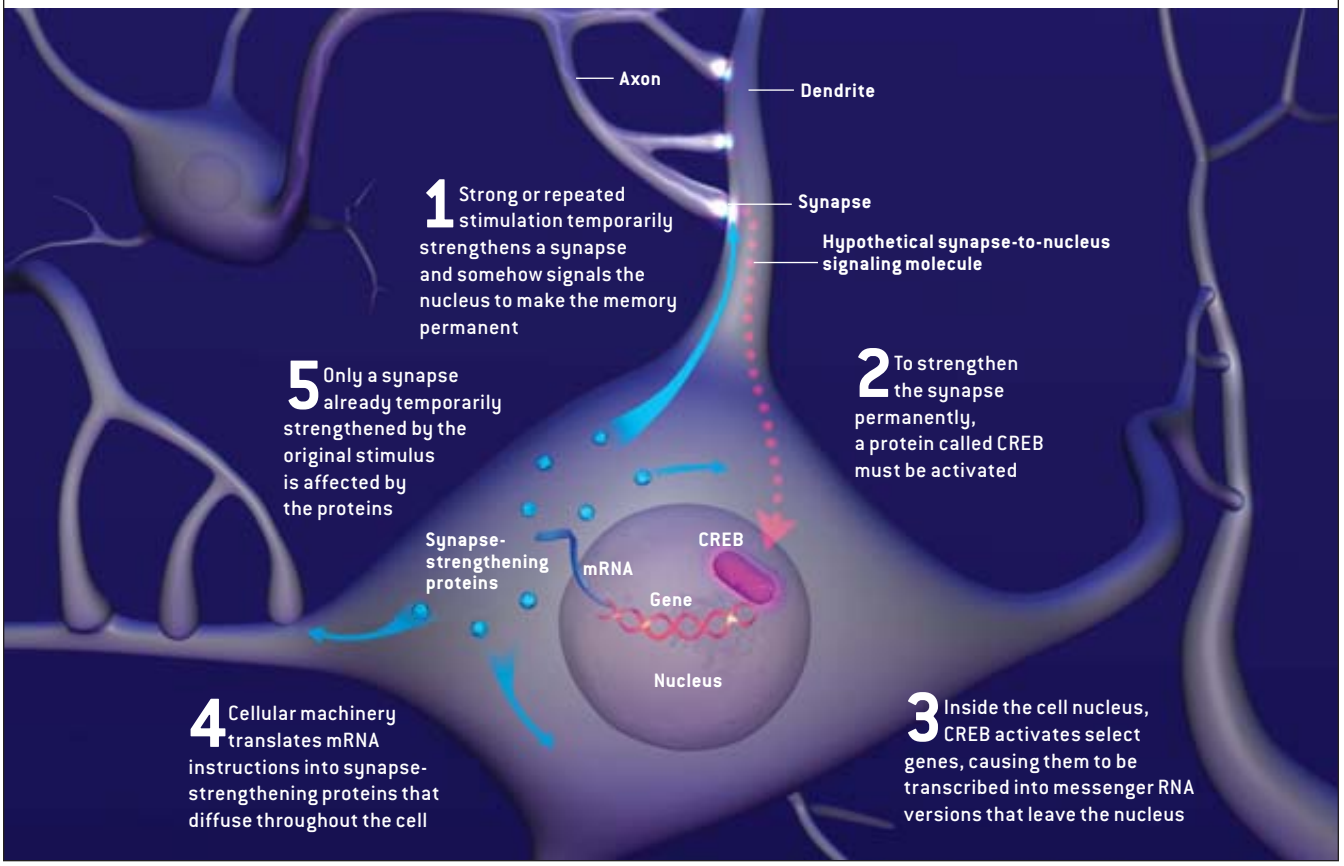
When a neuron receives such a signal, the voltage of the membrane on its dendrite changes slightly in the positive direction. This local change in voltage is described as a "firing" of the neuron's synapse. When a synapse fires in brief, high-frequency bursts, the temporary strengthening observed in short-term memory formation occurs. But a single

ALFRED T. KAMAJIAN

## HOW GENES MAKE MEMORIES STICK

That gene activation leading to protein manufacture is necessary for long-term memory formation was discovered in the 1960s. But this realization raised further questions: How does a gene in the nucleus "know" when to generate the proteins that permanently strengthen a synapse, thereby turning a short-term memory into a long-term one, and when to remain silent, allowing the short-term memory to simply fade away? Is there an undiscovered synapse-to-nucleus signaling molecule that tells the cell when to make synapse-strengthening proteins?

And once these proteins are manufactured in the cell body, how do they "know" which synapse among thousands to strengthen? By the mid-1990s, elegant experiments had provided some answers to the puzzle.




synapse firing briefly is generally not enough to make the neuron fire an impulse, technically termed an action potential, of its own. When many of the neurons' synapses fire together, however, their combined effort changes the voltage of the neuronal membrane enough to make the neuron fire action potentials and relay the message on to the next neuron in the circuit.

Hebb proposed that, like an orchestra player who cannot keep up, a synapse on a neuron that fires out of sync with the other inputs to the neuron will stand out as odd and should be eliminated, but synapses that fire together—enough so as to make the neuron fire an action potential—should be strengthened. The brain would thus wire itself up in accordance with the flow of impulses through developing neural circuits, refining the original general outline.

Moving from Hebb's theory to sorting out the actual mechanics of this process, however, one again confronts the fact that the enzymes and proteins that strengthen or weaken synaptic connections during brain wiring must be synthesized from specific genes. So our group set out to find the signals that activate those genes.

Because information in the nervous system is coded in the pattern of neural impulse activity in the brain, I began with an assumption that certain genes in nerve cells must be turned on and off by the pattern of impulse firing. To test this hypothesis, a postdoctoral fellow in my lab, Kouichi Itoh, and I took neurons from fetal mice and grew them in cell culture, where we could stimulate them using electrodes in the culture dish. By stimulating neurons to fire action potentials in different patterns and then measuring the amount of mRNA from genes known to be important in forming neural circuits or in adapting to the environment, we found our prediction to be true. We could turn on or off particular genes simply by dialing up the correct stimulus frequency on our electrophysiological stimulator, just as one tunes into a particular radio station by selecting the correct signal frequency.

ALFRED T. KAMAJIAN

## Time Code

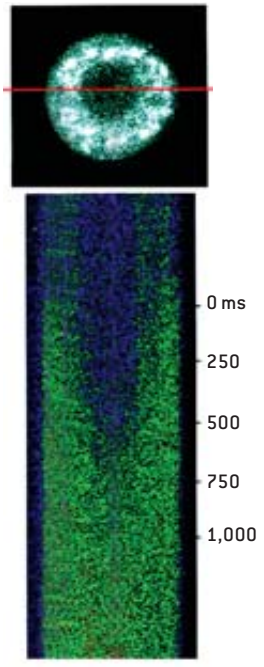
ONCE WE OBSERVED that neuronal genes could be regulated according to the pattern of impulses the cell was emitting, we wanted to investigate a deeper question: How could the pattern of electrical depolarizations at the surface of the cell membrane control genes deep in the nucleus of the neuron? To do so, we needed to peer into the cell cytoplasm and see how information was translated on its way from the surface to the nucleus.

What we found was not a single pathway leading from the neuron's membrane to its nucleus but rather a highly interconnected network of chemical reactions. Like the maze of roads leading to Rome, there were multiple intersecting biochemical pathways crisscrossing as they carried signals from the cell membrane throughout the cell. Somehow electrical signals of varying frequencies on the membrane flowed through this traffic in the cytoplasm to reach their proper destination in the nucleus. We wanted to understand how.

The primary way that information about the neuronal membrane's electrical state enters this system of chemical reactions in the cytoplasm is by regulating the influx of calcium ions through voltage-sensitive channels in the cell membrane. Neurons live in a virtual sea of calcium ions, but inside a neuron the concentration of calcium is kept extremely low—20,000 times lower than the concentration outside. When the voltage across the neuronal membrane reaches a critical level, the cell fires an action potential, causing the calcium channels to open briefly. Admitting a spurt of calcium ions into the neuron with the firing of each neural impulse translates the electrical code into a chemical code that cellular biochemistry inside the neuron can understand.

In domino fashion, as calcium ions enter the cytoplasm, they activate enzymes called protein kinases. Protein kinases turn on other enzymes by a chemical reaction called phosphorylation that adds phosphate tags to proteins. Like runners passing the baton, the phosphate-tagged enzymes become activated from a dormant state and stimulate the activity of transcription factors. CREB, for instance, is activated by calcium-dependent enzymes that phosphorylate it and inactivated by enzymes that remove the phosphate tag. But there are hundreds of different transcription factors and protein kinases in a cell. We wanted to know how a particular frequency of action potential firing could work through calcium fluxes to reach the appropriate protein kinases and ultimately the correct transcription factors to control the right gene.

By filling the neurons with dye that fluoresces green when the calcium concentration in the cytoplasm increases, we were able to track how different action-potential firing patterns translated into dynamic fluctuations in intracellular calcium. One simple possibility was that gene transcription might be regulated by the amount of calcium rise in a neuron, with different genes responding better to different levels of calcium. Yet we observed a more interesting result: the amount of calcium increase in the neuron was much less important in regulating specific genes than the temporal patterns of calcium flashes, echoing the temporal code of the neural impulse that had generated them.




CALCIUM IONS glow in a cross section of a neuron (*left, with dark nucleus at center*) filled with calcium-sensitive dye. The author used scanning laser confocal microscopy to track pulses of calcium influx following each action potential fired by the cell. Cross sections of the first view taken at two-millisecond intervals, then stacked (*below left*), provided a time-lapse representation of intracellular calcium density (*green* and *red*).

Another postdoc in my lab, Feleke Eshete, followed these calcium signals to the enzymes they activate and the transcription factors those enzymes regulate, and finally we began to appreciate how different patterns of neural impulses could be transmitted through different intracellular signaling pathways. The important factor was time.

We found that one could not represent the pathway from the cell's membrane to its DNA in a simple sequence of chemical reactions. At each step, starting from calcium entering the membrane, the reactions branched off into a highly interconnected network of signaling pathways, each of which had its own speed limits governing how well it could respond to intermittent signals. This property determined which signaling pathway a particular frequency of action potentials would follow to the nucleus.

Some signaling pathways responded quickly and recovered rapidly; thus, they could react to high-frequency patterns of action potentials but could not sustain activation in response to bursts of action potentials separated by long intervals of inactivity. Other pathways were sluggish and could not respond well to rapid bursts of impulses, but once activated, their slowness to inactivate meant that they could sustain signals between bursts of action potentials that were separated by long intervals of inactivity. The genes activated by this pathway would therefore respond to stimuli that are delivered repeatedly, but infrequently, like the repetition necessary for committing new information to memory.

In other words, we observed that signals of different temporal patterns propagated through distinct pathways that were favorably tuned to those particular patterns and ultimately regulated different transcription factors and different

THE AUTHOR

*R. DOUGLAS FIELDS* is chief of the Nervous System Development and Plasticity Section of the National Institute of Child Health and Human Development and adjunct professor in the Neurosciences and Cognitive Science Program at the University of Maryland. His last article in *Scientific American,* "The Other Half of the Brain" (April 2004), described the importance of glial cells to thinking and learning.

FROM FELEKE ESHETE AND R. DOUGLAS FIELDS IN *JOURNAL OF NEUROSCIENCE*, VOL. 21, NO. 17, SEPTEMBER 1, 2001. © SOCIETY FOR NEUROSCIENCE

genes. For instance, our measurements showed that CREB was rapidly activated by action potentials but sluggish in inactivating after we stopped stimulating the neuron. Thus, CREB would sustain its activation between repeated bursts of stimuli separated by intervals of 30 minutes or more, similar to the intervals of time between practice sessions required to learn new skills or facts.

Given CREB's role in memory, we could not help but wonder if the signaling pathway we were studying to understand brain development might not also be relevant to the mechanism of memory. So we devised a test.

## Memory in a Dish

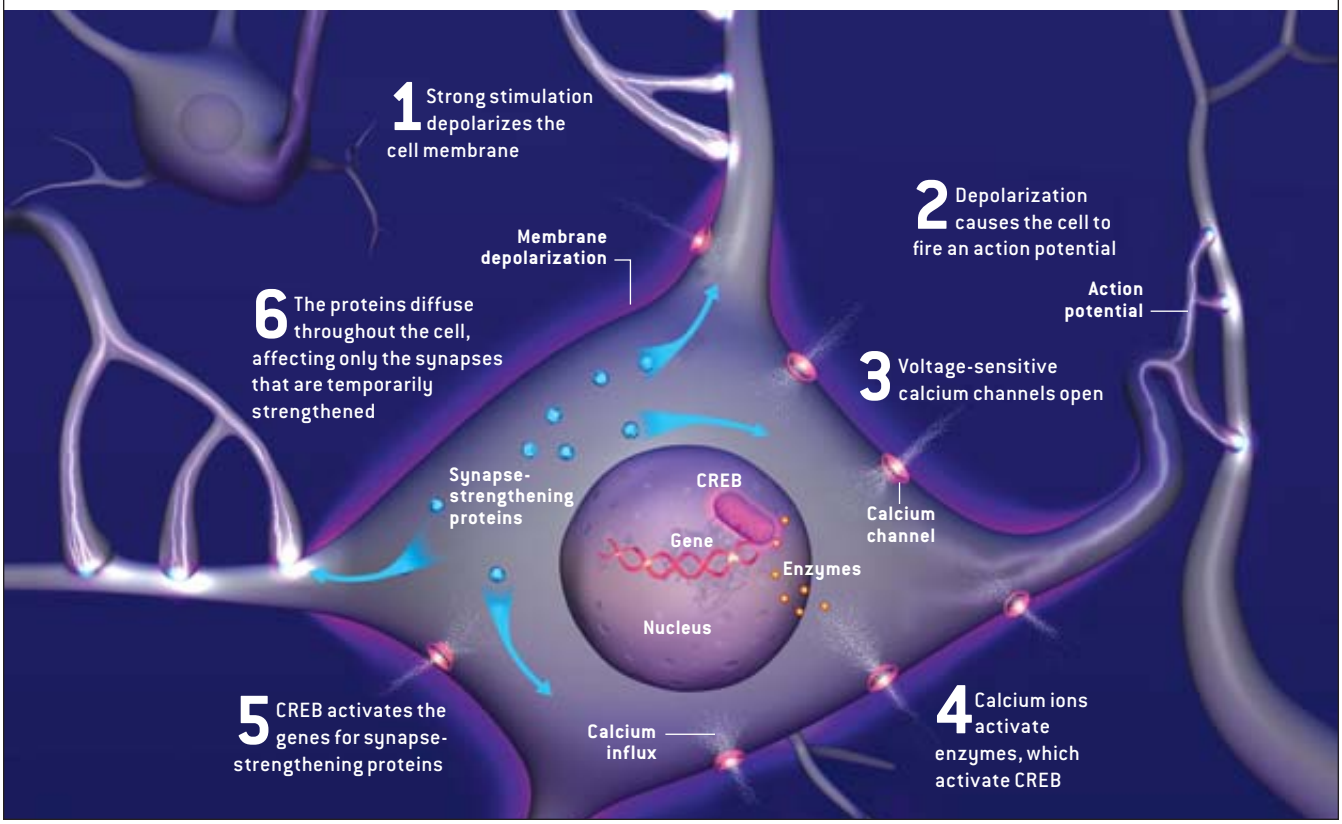
IF THE PART OF THE BRAIN that was removed from the patient HM, the hippocampus, is dissected from a rat and kept alive in a salt solution, microelectrodes and electronic amplifiers can record the electrical impulses from individual synaptic connections on a neuron. By administering a burst of electrical shocks to a synapse, causing it to fire in a specific pattern, that synaptic connection can be strengthened. That is to say, the synapse produces about twice as much voltage in response to subsequent stimulations after it has received the high-frequency stimulus.

This increased strength, termed long-term potentiation (LTP), can be, despite its name, relatively short-lived. When test pulses are applied at a series of intervals after the high-frequency stimulus, the voltage produced by the synapse slowly diminishes back to its original strength within a few hours. Known as early LTP, this temporary synaptic strengthening is a cellular model of short-term memory.

Remarkably, if the same high-frequency stimulus is applied repeatedly (three times in our experiments), the synapse becomes strengthened permanently, a state called late LTP. But the stimuli cannot be repeated one after the other. Instead each stimulus burst must be spaced by sufficient intervals of inactivity (10 minutes in our experiments). And adding chemicals that block mRNA or protein synthesis to the salt solution bathing the brain slice will cause the synapse to weaken to its original strength within two to three hours. Just as in whole organisms, the cellular model of short-term memory is not

## HOW GENES "KNOW" WHEN TO STRENGTHEN A SYNAPSE

Experiments by the author show that a theoretical synapse-to-nucleus signaling molecule is unnecessary. Strong stimulation, either from the repeated firing of a single synapse or from the simultaneous firing of several synapses on a cell, depolarizes the cell membrane, causing the cell to fire action potentials of its own, which in turn causes voltage-sensitive calcium channels to open. The calcium ions interact with enzymes that activate the transcription factor CREB, which activates the genes for manufacturing synapse-strengthening proteins. The cell's nucleus "listens," in effect, to the cell's output—firing action potentials—to determine when to permanently strengthen a synapse and make a memory last.




ALFRED T. KAMAJIAN

dependent on the nucleus, but the long-term form of memory is.

Indeed, Frey and Morris had used this technique to show that synapse-strengthening proteins would affect any temporarily strengthened synapse. First, they stimulated a synapse briefly to induce early LTP, which would normally last just hours. Then they fired a second synapse on the same neuron in a manner that would induce late LTP in that synapse: three bursts separated by 10 minutes. As a result, both synapses were permanently strengthened. The stronger stimulus sent a signal to the nucleus calling for memory-protein manufacture, and the proteins "found" any synapse that was already primed to use them.

**FINALLY, WE BEGAN TO APPRECIATE THAT THE IMPORTANT FACTOR WAS TIME**

Based on our work showing how different patterns of impulses could activate specific genes, and recalling Hebb's theory that the *firing* of a neuron was critical in determining which of its connections will be strengthened, we asked whether a signaling molecule sent from the synapse to the nucleus was really necessary to trigger long-term memory formation. Instead we proposed that when a synapse fired strongly enough or in synchrony with other synapses so as to make the neuron fire action potentials out its axon, calcium should enter the neuron directly through voltage-sensitive channels in the cell body and activate the pathways we had already studied leading to CREB activation in the nucleus.

To test our theory, postdoc Serena Dudek and I administered a drug known to block synaptic function to the brain slice. We then caused neurons to fire action potentials by using an electrode to stimulate the neurons' cell bodies and axons directly. Thus, the neurons fired action potentials, but the synaptic inputs to these neurons could not fire. If a synapse-to-nucleus signaling molecule was necessary to trigger late LTP, our cellular model of long-term memory formation, then this procedure should not work, because the synapses were silenced by the drugs. On the other hand, if the signals to the nucleus originated from the neurons firing action potentials, as in our developmental studies, silencing the synapses should not prevent activation of the memory-protein genes in the nucleus.

We next processed the brain tissue to determine if the transcription factor CREB had been activated. Indeed, in the small region of brain slice that had been stimulated to fire action potentials in the complete absence of synaptic activity, all the CREB had a phosphate molecule added to it, indicating that it had been switched to the activated state.

We then checked for activity of the gene *zif268*, which is known to be associated with creation of LTP and memory. We found that it, too, was turned on by the hippocampal neuron firing, without any synaptic stimulation. But if we performed the same stimulation in the presence of another drug that blocks the voltage-sensitive calcium channels—which we suspected were the actual source of the signal from the membrane to the nucleus—we found that CREB phosphorylation, *zif268* and a protein associated with late LTP called MAPK were not activated after the neurons fired.

These results clearly showed that there was no need for a messenger from the synapse to the nucleus. Just as in our developmental studies, membrane depolarization by action potentials opened calcium channels in the neuronal membrane, activating signaling pathways to the nucleus and turning on appropriate genes. It seems to make good sense that memory should work this way. Rather than each synapse on the neuron having to send private messages to the nucleus, the transcriptional machinery in the nucleus listens instead to the output of the neuron to decide whether or not to synthesize the memory-fixing proteins.

## Molecular *Memento*

PERHAPS UNDISCOVERED synapse-to-nucleus signaling molecules do participate in some way in the memory process, but our experiments indicate that they are not absolutely necessary. As predicted by Hebbian rules of learning, the firing of a neuron, resulting from the combined excitation of all synaptic input to the cell, is the necessary event for consolidating memory.

This understanding offers a very appealing cellular analogue of our everyday experience with memory. Like Leonard in *Memento* or any witness to a crime scene, one does not always know beforehand what events should be committed permanently to memory. The moment-to-moment memories necessary for operating in the present are handled well by transient adjustments in the strength of individual synapses. But when an event is important enough or is repeated enough, synapses fire to make the neuron in turn fire neural impulses repeatedly and strongly, declaring "this is an event that should be recorded." The relevant genes turn on, and the synapses that are holding the short-term memory when the synapse-strengthening proteins find them, become, in effect, tattooed. SA

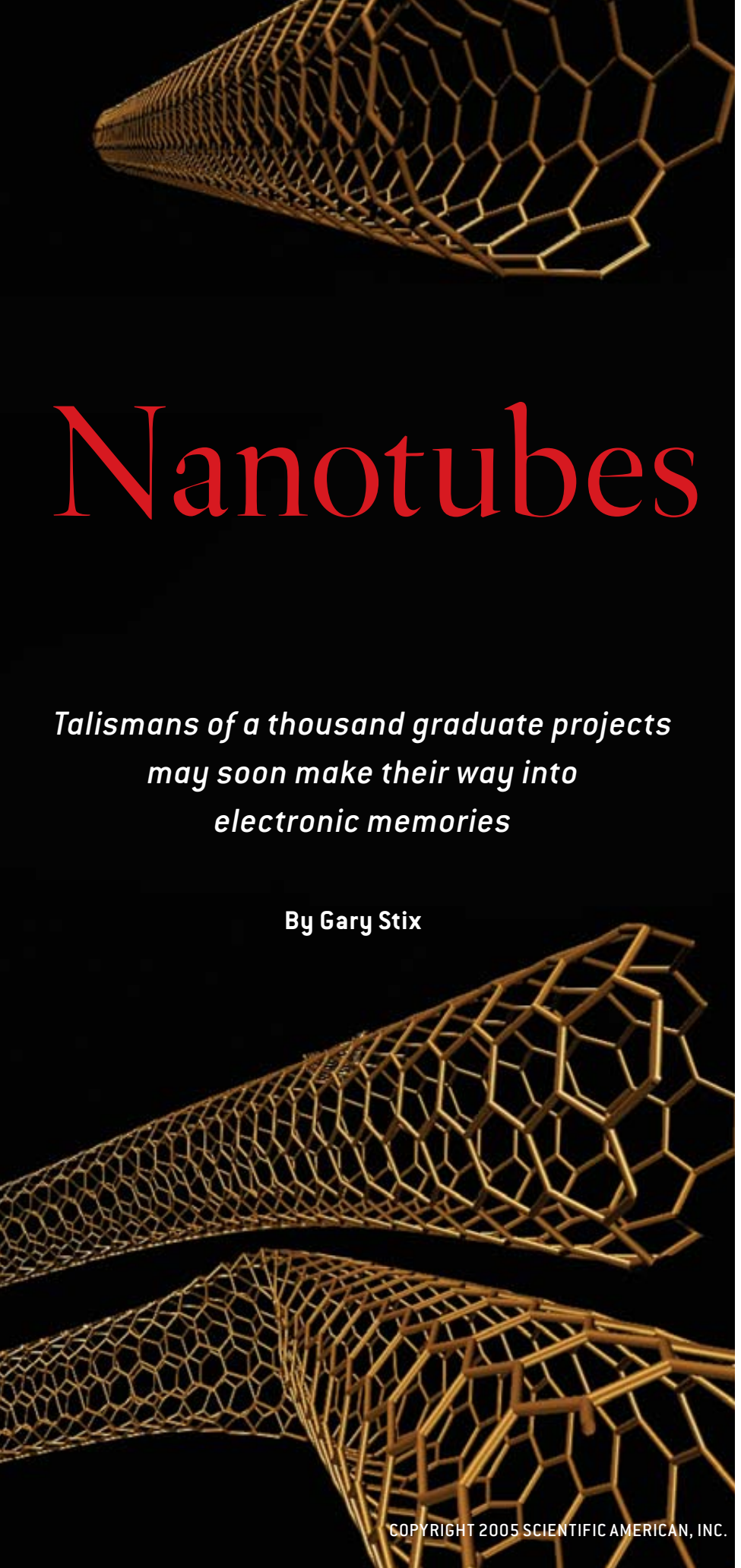
### MORE TO EXPLORE


**Regulated Expression of the Neural Cell Adhesion Molecule L1 by Specific Patterns of Neural Impulses.** Kouichi Itoh, B. Stevens, M. Schachner and R. D. Fields in *Science,* Vol. 270, pages 1369–1372; November 24, 1995.

**Synaptic Tagging and Long-Term Potentiation.** Uwe Frey and Richard G.M. Morris in *Nature,* Vol. 385, pages 533–536; February 6, 1997.

**Somatic Action Potentials Are Sufficient for Late-Phase LTP-Related Cell Signaling.** Serena M. Dudek and R. Douglas Fields in *Proceedings of the National Academy of Sciences USA,* Vol. 99, No. 6, pages 3962–3967; March 19, 2002.

**Memory Systems of the Brain: A Brief History and Current Perspective.** Larry R. Squire in *Neurobiology of Learning and Memory,* Vol. 82, pages 171–177; November 2004.



# Nanotubes in the Clean Room

*Talismans of a thousand graduate projects may soon make their way into electronic memories*

**By Gary Stix**



Charles M. Lieber, a major figure in nanotechnology, asked one of his graduate students in 1998 to undertake the design of a radically new type of computer memory. It would read and write digital bits with memory elements that measured less than 10 billionths of a meter (10 nanometers). Until then, the student, a German native named Thomas Rueckes, had been spending his time in Lieber's laboratory at Harvard University measuring the electrical and material properties of carbon nanotubes. These cylinders, measuring but a nanometer or so in diameter, display a surface of hexagonal carbon rings that give the material the appearance of a honeycomb or chicken wire. Since the discovery of nanotubes in 1991, the scientific community has lauded them for their superlative material and electrical properties.

Lieber wanted to know whether Rueckes could come up with a concept involving nanotubes that could be submitted for funding under a molecular electronics program funded by the Defense Advanced Research Projects Agency. Rueckes pored over books and review articles for a few days, but nothing good suggested itself. One evening he left the chemistry lab and crossed the street to the

cafeteria at the Harvard Science Center. On his pizza run, he passed the Harvard Mark 1, the 55-foot-long monstrosity, a predecessor of modern computers, that had served the U.S. Navy as a calculator for gunnery and ballistic computations until 1959. It now decorated the center's hallway. Back in the lab, he remembered that the Mark 1 operated by moving mechanical relays from one position to another. "That is what flipped a switch in my brain," he remembers. "I could see a picture of how to build a memory."

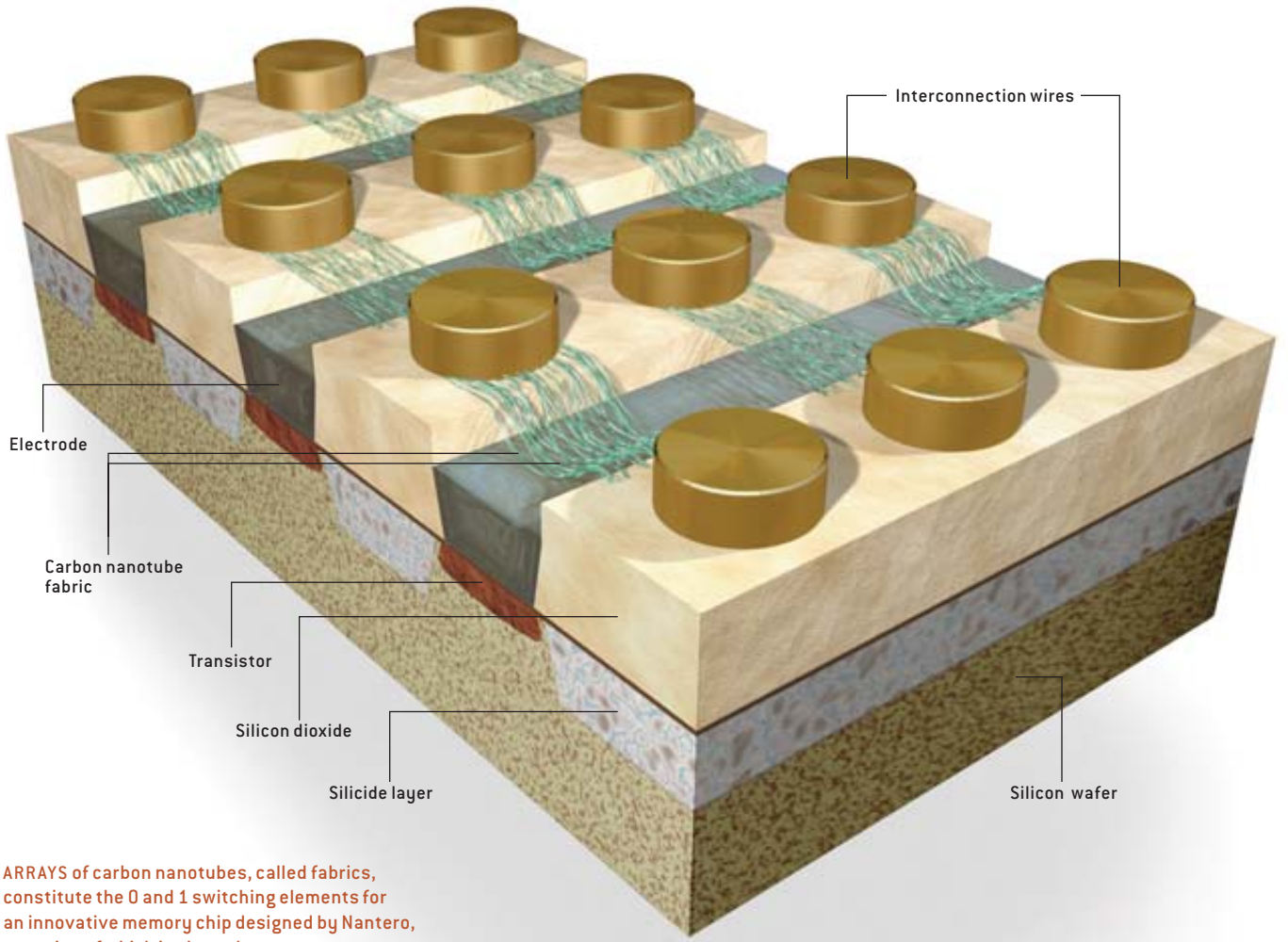
Many researchers were trying to use nanotubes as wires or components in new transistor designs. The Mark 1 inspiration prompted Rueckes to focus instead on their extraordinary tensile strength and resilience. Nanotubes, he imagined, might flex up and down to represent a 0 and a 1 state, like hyper-shrunken versions of the relays in the Mark 1. "We sat down and worked out a proposal in a couple of days and submitted it to DARPA, and they funded it in one day," Rueckes says.

Until his graduation in 2001, Rueckes continued to develop the concept. As he worked, he realized that nanotubes had more and more to offer. They could, in theory, provide the makings of a universal memory, one that combined the speed of static random-access memory, the low cost of dynamic random-access memory (DRAM), and the nonvolatility (instant-on operation) of flash memory. Its status as *uber*-material would also make it a low consumer of electrical power as well as resistant to potentially damaging heat, cold and magnetism.

## When Billionths Meet Trillions

ON PAPER, the design was relatively simple. Nanotubes would serve as individually addressable electromechanical switches arrayed across the surface of a microchip, storing hundreds of gigabits of information, maybe even a terabit. An electric field applied to a nanotube would cause it to flex downward into a depression etched onto the chip's surface, where it would contact another nanotube (in current designs, it touches a metal electrode). Once bent, the nanotubes could remain that way, including when the power was turned off, allowing for nonvolatile operation. Van der Waals forces, which are weak molecular attractions, would hold the switch in place until application of a field of different polarity caused the nanotube to return to its straightened position.

Even before Rueckes had finished at Harvard, he received a visit from an executive at an Internet company who was looking to strike out in a new direction.




ARRAYS of carbon nanotubes, called fabrics, constitute the 0 and 1 switching elements for an innovative memory chip designed by Nantero, a section of which is shown here.

JEAN-FRANCOIS POVEDIN

Greg Schmergel, a Harvard M.B.A. and former management consultant, had come to learn through his experience as an Internet entrepreneur about the fickleness of the new medium and how low the barriers for new entrants were. His company, a successful venture called ExpertCentral.com, which provided professional services references, had experienced these vicissitudes firsthand. It was scooped up by About.com, which, in turn, was bought by Primedia.

Nanotechnology seemed less amenable to dot-com-style feeding frenzies. Most people, even scientists, could not offer a cogent definition, except to point to the science-fiction section at Barnes & Noble. Schmergel did not know all that much about it either, although it did seem as faraway from an Internet company as anything he could imagine. But Schmergel, who was also heir to a long tradition of entrepreneurship (his father started one of the first biotech companies), did know business, whereas Rueckes understood, as well as anyone could, the emerging field of nanotechnology.

So, in 2001, Schmergel and Rueckes, along with Brent M. Segal, another former Harvard chemistry doctoral student, formed Nantero, a name whose genesis again combined the small ("nano") and the large ("tero," a corruption of "tera," or trillions, as in trillions of bits). Lieber himself opted to pursue more advanced projects in his Harvard lab, smart nanowires that would assemble on their own into finished devices and that might use biological or other unorthodox signals for communication among device structures.

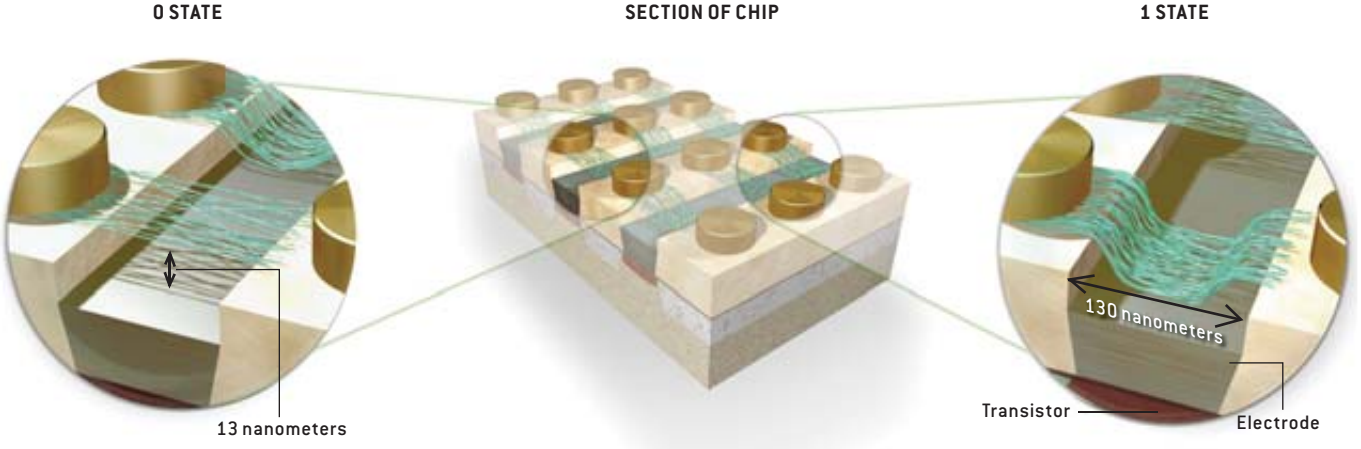
The immediate mandate for Nantero was to move beyond an advanced graduate project to create a device that could be manufactured in a working semiconductor facility. The company set up shop in a Woburn, Mass., industrial park populated largely by biotechnology firms. Schmergel tried to remove as many distractions as possible for his researchers: Nantero is still not listed in the Woburn telephone directory. Early on the team approached a number of big chip manufacturers. Engineers there did not always greet their presentations warmly. Rueckes recalls how one manager sputtered: "We don't want your virus in our plant."

## Ironing Things Out

NANOTUBES, purchased from bulk suppliers, are a form of high-tech soot that contains a residue that averages 5 percent iron, a contaminant whose very mention can produce involuntary tremors in managers of multimillion-dollar clean rooms. The Nantero team devoted much of its early development to devising a complex filtration process to reduce the amount of iron to the parts-per-billion level.

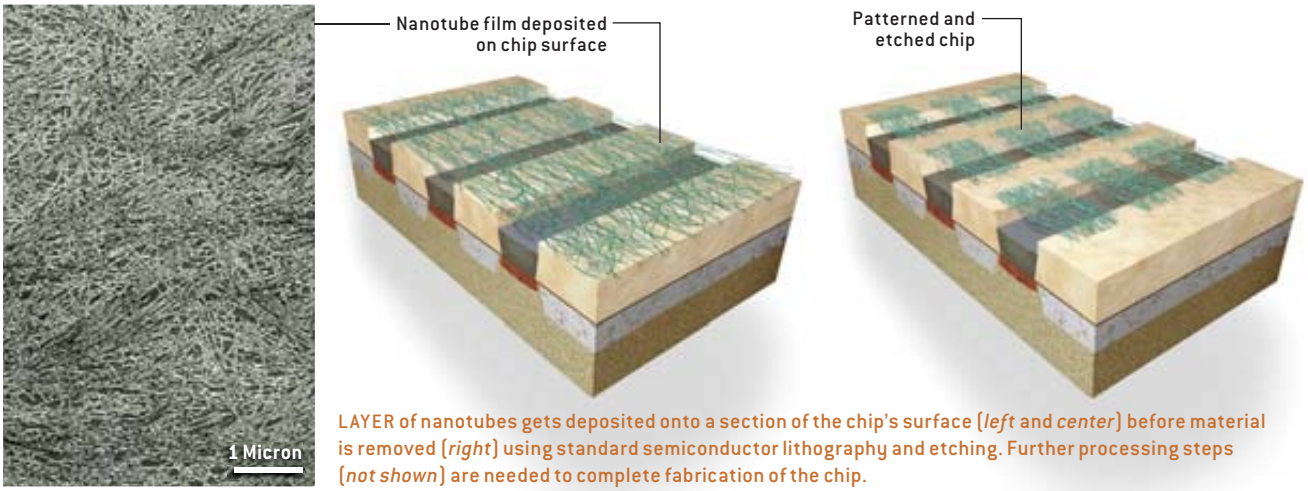
Adapting rolled-carbon chicken wire to the standard photolithography and etching process that patterns and removes material to form electrical circuitry proved just as daunting. New chip factories cost more than $2 billion, and notoriously conservative plant managers had no inclination to retool to integrate nanotubes into the standard CMOS (complementary metal oxide semiconductor) manufacturing process. When Nantero started, no good options existed for forming a nanotube on the surface of a wafer (the round silicon disk from which chips are carved) without interfering with adjoining electrical circuitry. Deposition of nanotubes onto the wafer using a gas vapor required temperatures so high that the circuitry already in place would be ruined. Alternatively, coating the wafer with a nanotube-containing solvent by spinning the disk like a phonograph record also had its problems. A suitable solvent, chlorobenzene, was considered excessively toxic and had been banned from chip factories.

Nantero devised a proprietary solvent suitable for spin coating. The thin film of nanotubes left after the solvent is removed can be subjected to lithography and etching that leaves the surface of the wafer with evenly spaced groupings of nanotubes. On close inspection, the conglomeration of threadlike nanotubes resembles a helter-skelter unwoven fabric. An electric field applied to one of the fabric elements bends it downward until it contacts an electrode, a position that represents a digital 1. ASML, a major semiconductor tool manufacturer, helped to refine this process with Nantero.




SAGGING AND STRAIGHTENING represent the 1 and 0 states for a random-access memory made up of groupings of nanotubes. In its 0 state, the fabric remains suspended above the electrode (*left*). When a transistor turns on, the electrode produces an electric field that causes a nanotube fabric to bend and touch an electrode, a configuration that denotes a 1 state (*right*).

JEAN-FRANCOIS POVEDIN




LAYER of nanotubes gets deposited onto a section of the chip's surface (*left* and *center*) before material is removed (*right*) using standard semiconductor lithography and etching. Further processing steps (*not shown*) are needed to complete fabrication of the chip.

When Nantero had gained confidence with the technology, it began a new round of visits to semiconductor manufacturers. In 2003 LSI Logic, a leading maker of customized chips for the telecommunications, storage and consumer electronics industries, agreed to bring the process for making what Nantero calls nanotube random-access memory (NRAM) into its factory in Gresham, Ore. To everyone's surprise, the collaborators had a working prototype within nine months. The project was quickly put on an early-development track, targeting the first commercial production memories for 2006. "I'm still amazed that the darn things work, because I was a little skeptical," says Norm Armour, general manager for the Gresham plant. LSI is interested in pursuing the technology as a replacement for fast-access memory modules (static RAM) embedded on microprocessors that consume an ever larger part of the chip area. A nanotube memory could be faster and much smaller while consuming less power.

In coming months, LSI and Nantero will strive to increase "yield," the ability to make millions of nanotube memories with near-perfect repeatability. To achieve high yields, engineers must attend to a multitude of details. If, for instance, the cavity over which the nanotube is suspended does not form sharp enough edges, it can adversely affect the device's electrical characteristics, changing the voltage at which it turns on and off. "The yield question is a big question, but we don't see anything insurmountable," comments Verne Hornback, LSI's senior project manager on the Nantero collaboration.

Although nanotube memories have intrigued the industry, skepticism remains. "Nantero has a great idea, but I believe it is a long way from having a credible manufacturing process," says G. Dan Hutcheson, who heads the market analysis firm VLSI Research in Santa Clara, Calif. He adds: "I will be very surprised if Nantero can make a scaled-up device that can compete cost-effectively with a DRAM as they claim, because I doubt that their process is scalable and repeatable. So the yields will be low."

A leader in this area of research, IBM has not pursued nanotube memories. The company has decided to focus on using nanotubes to replace a critical component that shuttles electrons from one side of a transistor to another. "We have no problems in finding choices for memory, but we're running out of choices for logic. And nanotubes offer unique properties for logic," observes Phaedon Avouris, a scientist at the IBM Thomas J. Watson Research Center.

Of course, Nantero thinks that the development work with LSI this year will disprove the doomsayers—for instance, the use of nanotube fabrics instead of the individual nanotubes as switching elements, which was an approach employed in the early design at Harvard, mitigates concerns about variability in size among the tubes. And the company has already attracted another partner, BAE Systems, to work on defense and aerospace applications for the radiation-resistant NRAMs. Even if the chips do not meet expectations, Nantero, which has filed for 60 patents and been granted 10 of those applications, will be left with valuable manufacturing know-how that could be licensed to others who want to combine nanotubes with chipmaking.

Just getting nanotubes into a factory at all marks a milestone. "The biggest victory we've had is to bring the process into a standard CMOS facility," LSI's Hornback remarks. A nanotube chip in a cell phone would be sweet vindication for the legions of researchers who have spent the early part of their careers poking and shocking these invisible specks. Until now, virtually the only products that incorporate this material that is stronger than steel and as hard as diamond have been glowing press releases from universities and industry. SA

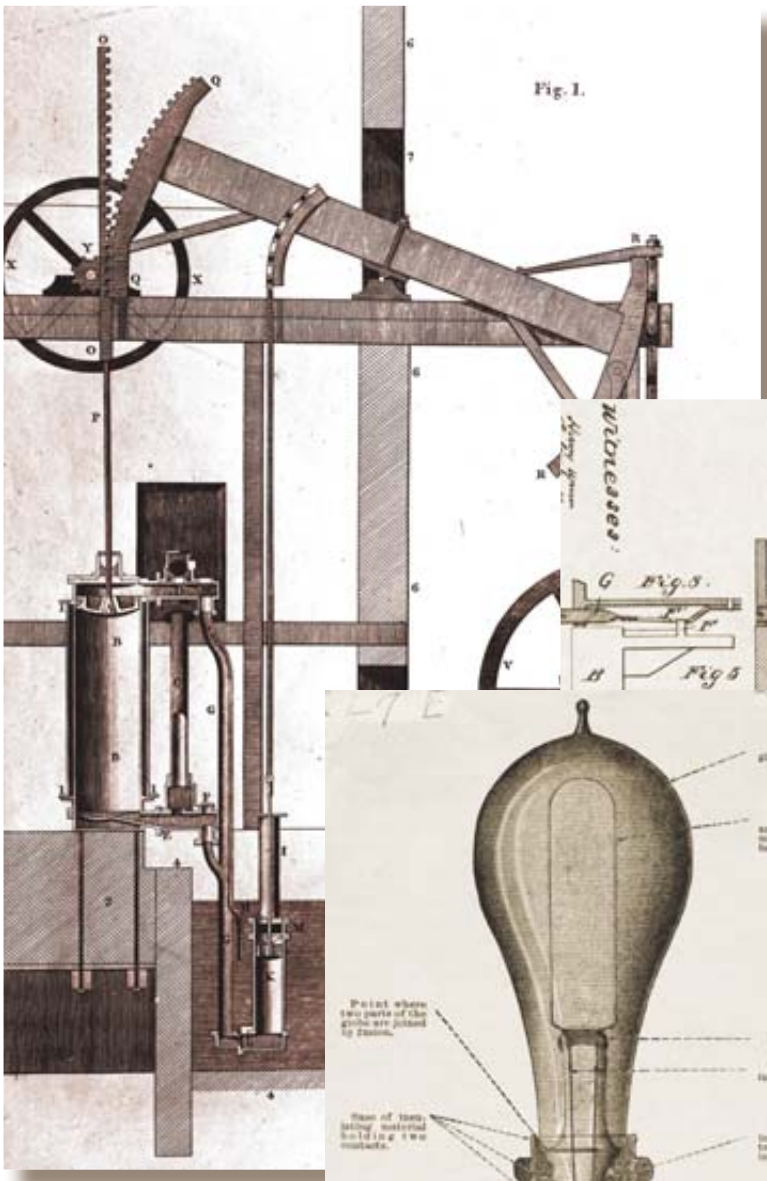
## MORE TO EXPLORE

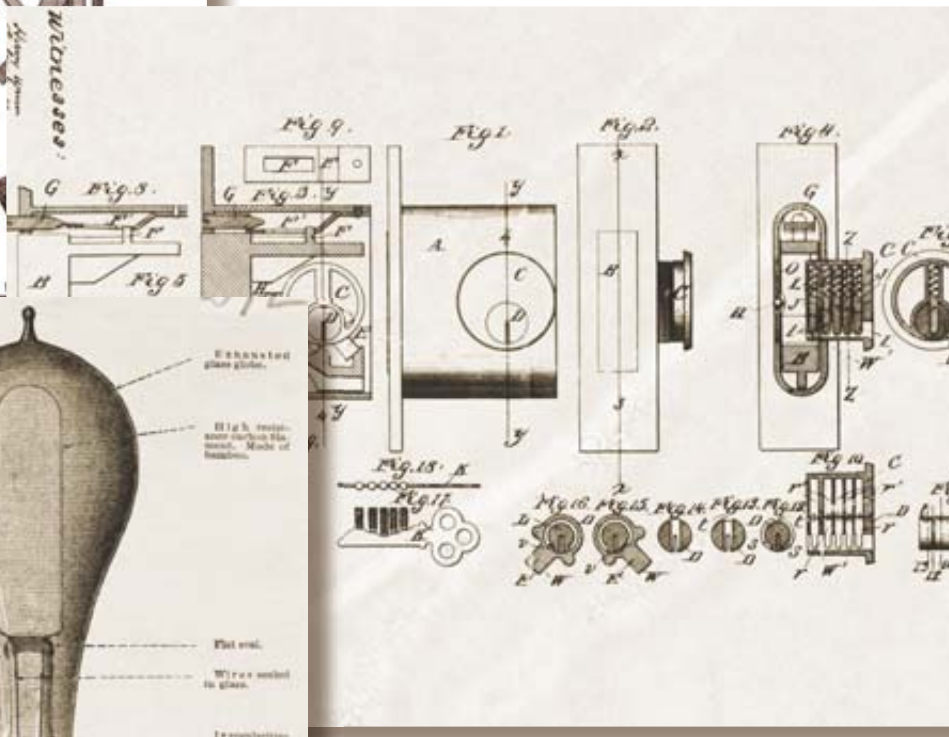
**The Incredible Shrinking Circuit.** Charles M. Lieber in *Scientific American,* Vol. 285, No. 3, pages 58–64; September 2001.

**Supertubes.** Phaedon Avouris in *IEEE Spectrum,* Vol. 41, No. 8, pages 40–45; August 2004.

Information about Nantero and NRAMs can be accessed at **www.nantero.com**

NANOTERO (*left*); JEAN-FRANCOIS POVEDIN (*center* and *right*)

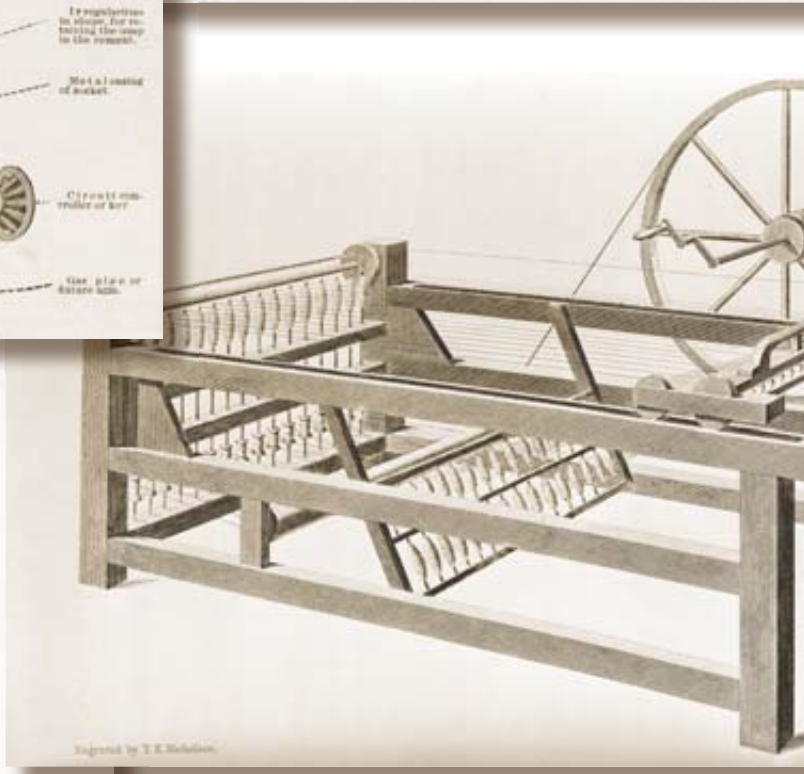






THE EDISON LAMP.



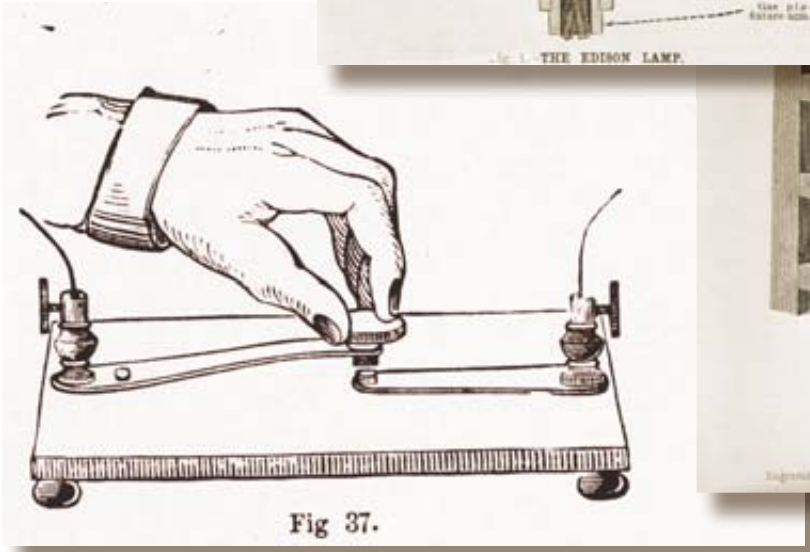


Fig 37.

INNOVATION IS ALIVE AND KICKING ON CAMPUS

# THE NEW College Try

BY STEVE MIRSKY

WINNERS of the 2004 Collegiate Inventors Competition. From left to right: Undergraduate Prize winner Wei Gu; Graduate Prize co-winner Jwa-Min Nam; Grand Prize winner Ozgur Sahin; Graduate Prize co-winner Colby Shad Thaxton.

**ON OCTOBER 2, 2004, AN EXCEPTIONAL GROUP** of young people gathered at the National Inventors Hall of Fame in Akron, Ohio. They were there to stack up their inventions against proven winners, such as the cotton gin, the airplane and the polymerase chain reaction (PCR) for replicating DNA. The 19 undergraduate and graduate students were the finalists in the 14th annual Collegiate Inventors Competition.

Working solo or in teams of two or three, the 19 entrants represented five undergraduate and nine graduate projects. Those final 14 were the survivors of a process that began with the solicitation of applications from 800 colleges and universities worldwide, resulting in 120 submissions.

Judging was based on the invention's originality as well as on its potential value and usefulness. "There's a screening process where we bring in experts from all over, from universities, from private industries, from the patent office," explains Donald B. Keck, one of the final judges. Keck, the former executive director of research at Corning, is also one of the inventors of optical fiber—and a member of the Hall of Fame. "We divide the 120 submissions we had this year into selected disciplines," he explains. "And we have experts rate those and give us the top scores coming out of each of the areas."

After hearing oral presentations from the finalists, a multidis-

ciplinary panel of eight judges names winners in the undergraduate, graduate and grand prize categories. The undergraduate winner gets $15,000, the graduate winner receives $25,000 and the grand prize winner takes home $50,000. (The grand prize winner's faculty adviser also receives $10,000, with the other winners' advisers getting $5,000 each.) The U.S. Patent and Trademark Office is the competition's major sponsor.

"Companies would hire some of these folks in an instant," Keck comments. "These kids are the top students coming out of our universities—they are the cream of the crop." The winners, as well as all the finalists, display the necessary qualities of the successful inventor—ample amounts of inspiration, determination and perspiration.

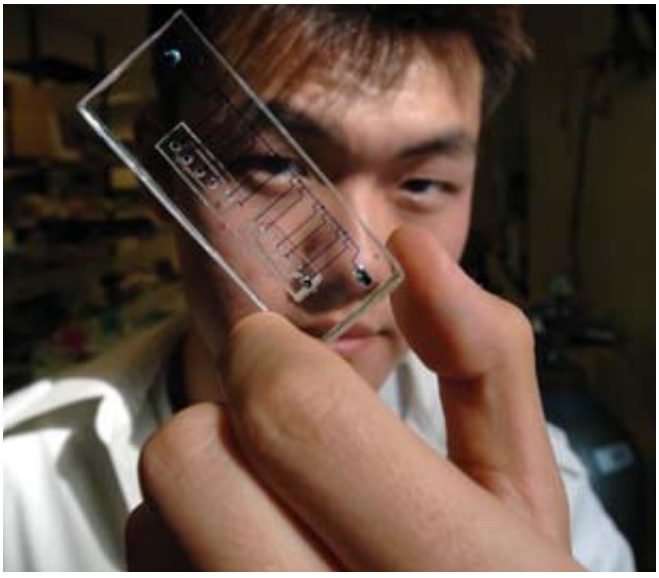
## MAKING THE FLOW GO

**Undergraduate Prize Winner:** Wei Gu, University of Michigan at Ann Arbor

**Adviser:** Shuichi Takayama, Department of Biomedical Engineering

**Invention:** A convenient system for controlling the flow of fluids through microscopically thin channels—based on a 30-year-old gadget for outputting in Braille

**Application:** Safer, faster testing of new drug compounds



WEI GU gazes at a silicone rubber microfluidic chip.

Wei Gu used an old Braille device to spell the solution to a new problem. The 21-year-old undergraduate student at the University of Michigan programmed it to control the flow of fluid in minuscule channels carved into flexible silicone rubber chips. The system has been compared to an integrated circuit for microfluidic flow. Among its potential uses is a better way to test new drugs on human cells before clinical trials.

Gu was born in Shanghai. In 1989 he and his mother emigrated to Canada, where his father was pursuing a doctoral degree, shortly after tanks rolled through Tiananmen Square. The family moved on to the U.S. six years later. Gu was in the sixth grade when he began to hint at his future: while most kids were playing computer games, he was learning how to program them.

Although he assumed he would enter the fields of computer science or electrical engineering, Gu was also interested in biology. Once at the University of Michigan, he began working in the laboratory of Shuichi Takayama, who was trying to use microfluidic technology to study cell behavior.

Soft silicone rubber chips are about the size of a credit card. They basically consist of a thin slab of silicone rubber that has had small channels etched onto it, sealed off with another thin slab of silicone rubber. (The channels are truly tiny: they can be as little as 0.05 millimeter wide and one tenth that deep.) Controlling the flow of fluid through the channels was cumbersome.

"There were methods to control flow," Gu explains. "But they were either driven by gravity, by which you only have a unidirectional flow from whatever's higher to whatever's lower, or by pressure generated with a syringe pump, where there's a source syringe." The silicone rubber chip was thus infested with external control devices. "So it was either a lack of flexibility or a lack of accessibility," Gu says.

Takayama hit on the idea of the old Braille pin readers as a possible control system. These readers consisted of a forest of motorized pins, each of which could be raised and lowered. The device's software drove pin movement, translating text on a computer screen into familiar Braille letters—thereby allowing blind people to use computers much more easily. Gu fished a pin reader out of a closet at the university's center for disabled students and examined it. Using a 486 computer rescued from his family's garage, outdated software and the discarded Braille display, Gu took microfluidic flow control from Rube Goldberg to the *Goldberg Variations*—from awkward to elegant.

In Gu's device, the grid of vertically moving pins sits underneath the network of silicone-rubber channels. "When the pins move up against the channel, it squishes them shut, like stepping on a garden hose," Gu explains. "When this happens, it's essentially a valve. And when you have three of these valves in a sequence, you can peristaltically pump inside of these channels. So when you have a grid of these pins, you

NATIONAL INVENTORS HALL OF FAME (*winners*) AND BETTMANN/CORBIS (*patent drawings*) (*preceding pages*); LON HORWEDEL *Ann Arbor News* (*left and opposite page*)

MOTORIZED PINS of a Braille pin reader control the flow of fluid in a microfluidic chip. For example, a single pin can be a valve—retracted in the reader, it allows fluid flow through the tiny channel, but in the upright position it impinges on the chip and stops fluid flow. Three adjacent pins moving up and down again in sequence can act as a pump, forcing fluid in the direction of choice.

essentially have a grid of valves and pumps, and with that you can accurately control fluid inside of our channels."

Gu hopes that this engineering feat quickly finds biological applications, such as in drug testing. His winning entry included additional published research on growing cell cultures within the microfluidic channels. "You could use human cells in vitro in a format that more closely simulates an in vivo situation," Gu says, "because you've arranged different compartments of human cells into a circulatory system much like a real human being." He adds: "You're trying to imagine what route the drug will take inside the human body and sending the drug through to see what happens. For example, you could see how a drug gets modified in the liver and then the effect on the next organ system. It could be a mini human on a chip."

## GOLDEN MEANS

**Graduate Prize Winners:** Jwa-Min Nam, University of California, Berkeley, and Colby Shad Thaxton, Northwestern University

**Adviser:** Chad Mirkin, professor of chemistry and director, Institute for Nanotechnology, Northwestern University

**Invention:** A new method for detecting and identifying trace amounts of biological molecules in complex samples

**Applications:** Medical testing; forensics; biological weapons detection; biochemical analysis

Crime scene investigators routinely use the PCR technique to detect and identify vanishingly small amounts of DNA at crime scenes. Jwa-Min Nam and Colby Shad Thaxton have developed a technique that does PCR one better: not only does it recognize DNA from only a few molecules in a sample, but it works the same trick with proteins. It opens a window for biologists onto an entirely new world of sample analysis.

They call their creation the biobarcode amplified detection system, which they developed with their adviser, Chad Mirkin. Nam is a 31-year-old chemist, originally from Seoul, South Korea. He is now doing postdoctoral research at the University of California at Berkeley. Thaxton is a 29-year-old physician who is also working on a Ph.D. in chemistry.

Their system accomplishes its needle-in-a-haystack task by, in a sense, giving up on trying to find the needle. Instead it searches for an easily spotted proxy molecule.

"The general concept," Thaxton explains, "is that we want to detect a protein or DNA sequence—some molecule that's floating around in solution. We take a magnetic particle. And on the surface of that magnetic particle there's a recognition element, something that recognizes whatever protein or DNA sequence we are interested in." In the case of DNA, the recognition element would be a complementary DNA sequence sure to attach itself to DNA in the sample. For finding proteins, the recognition element is an antibody.

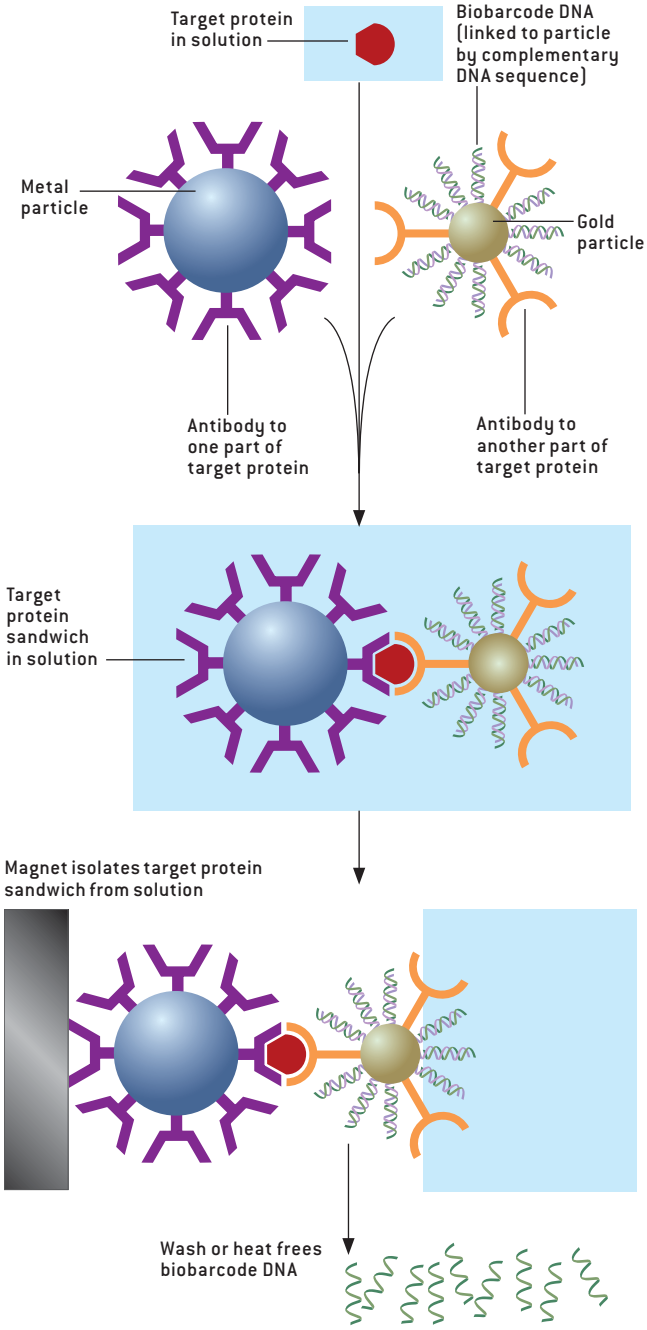
"The next step is to add another particle that also recognizes that same DNA or protein," Thaxton says. They use a speck of gold only 30 nanometers in diameter (10,000 of them could stretch across the period at the end of this sentence) that also displays a DNA sequence or antibody designed to latch onto another part of the targeted molecule. "So you form this little sandwich structure," Thaxton says, "where you have a magnetic particle, you have the molecule of interest, and then the gold particle stuck on the other side."

This sandwich system is practical because the gold nanoparticles are also covered with up to 800 copies of a specifically created, 40-nucleic-acid-residue-long DNA sequence. These sequences are the biobarcode: a known marker that identifies a sample, like a barcode with price and product information on a cereal box.

Exposing the sample to a magnetic field pulls the magnetic particles to one side for isolation. If any of the target molecules are present, they get dragged along, too, as do the gold nanoparticles festooned with biobarcodes. A simple wash with pure water detaches these biobarcodes, thousands of copies of which then exist freely in solution and are easy to detect. So the researcher looks for these biobarcode sequences, knowing that they signal the presence of the protein or DNA sequence truly sought.

Thaxton is planning on a career in urology, so one of the first tests the team tried was for prostate-specific-antigen (PSA), a marker for prostate cancer. Their system identified PSA with a million times the sensitivity of conventional assays. Thaxton, Nam, Mirkin and postdoctoral fellows Dimitra Georganopoulou and Savka Stoeva have also used the system to detect an early protein marker for Alzheimer's disease and to find anthrax DNA sequences, illustrating its potential as a biowarfare detection device. It could be designed to simultaneously find DNA sequences, RNA sequences and proteins. That capability would reveal whether a particular

gene's protein product is being made at a given time and in what amounts. Tomorrow's molecular medicine may track such expression profiles as routinely as today's medicine measures cholesterol and blood pressure.




BIOBARCODE technology finds minute traces of a target molecule in solution. In this example, the target is a protein. Antibodies that are attached to a metal particle and to a gold nanoparticle allow the formation of a "sandwich" that includes the target protein. A magnet attracting the metal particle then pulls the sandwich out of the solution. Washing or heating the isolated sandwich releases many copies of "biobarcode" DNA from the surface of the gold particle. These abundant biobarcodes are easier to detect than the small amount of protein.

## FORCE, TIME AND HARMONY

**Grand Prize Winner:** Ozgur Sahin, Stanford University

**Adviser:** Olav Solgaard, Department of Electrical Engineering

**Invention:** A new type of atomic-force microscope sensitive to the music of molecular interactions can study the physical properties of materials in exquisite detail

**Applications:** Research into new materials; detection of biological molecules

Ozgur Sahin grew up in Kayseri, Turkey, a city of about half a million people some two hours by car from Ankara. When he was 11, he surprised his parents with something he built from his Lego set: a mechanical adding machine. Now 25 and a doctoral candidate in electrical engineering in Olav Solgaard's laboratory at Stanford University, he probably no longer surprises his parents all that much, even when inventing an atomic-force microscope, or AFM. "It is a new kind of AFM that is targeted toward identifying materials at a very small scale rather than observing their shapes and topography," he explains.

AFM is a unique form of microscopy, because it depends on making physical contact with whatever sample is being examined. (Stanford's Calvin F. Quate, co-inventor of atomic-force microscopy in the 1980s, also advises Sahin.) A flexible silicon cantilever, the tip of which is only atoms wide, taps across a surface to scan it. Measurements of the various forces deflecting the tapping cantilever provide useful information about the surface's shape.

Existing AFMs, however, have limited resolution because the force measurements must be averaged over time. By analogy, in a dark room, your fingers feeling across a tabletop could easily identify a fork, a spoon, a dish and a coffee cup. But adding up and averaging your impressions of the objects on a table would yield a blurry assessment of the general topography—the precise shapes would be reduced to a few sticks, a disk and a mound. Sahin's invention takes advantage of inherent and designable properties of the cantilever to clear up the blur. And it can even reveal what materials the objects are made up of.

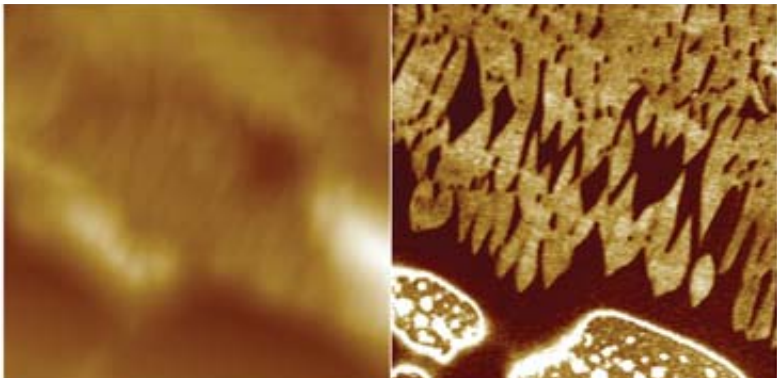
The cantilever taps across the surface with metronomic precision. But as it moves, it also behaves much like a tuning fork, producing overtones related to the fundamental vibration. "The higher harmonics are all driven by the forces acting on the cantilever tip," he and his colleagues wrote in a journal article. Years of work and design modification allowed Sahin to successfully channel the energy from one of those faster harmonic frequencies back into a wagging motion of the cantilever. Thus, the motions of the cantilever provide information about the forces on the surface over extremely brief intervals. "Instead of having a very dull tip in the time dimen-

LAURIE GRACE

sion," Sahin says, "I make it very sharp in the time dimension so that I can see time variations of the forces. The tip was already sharp in our three spatial dimensions, so basically I created a very sharp object in four dimensions to probe things both in space and in time."

Using this new AFM probe, researchers will be able to gather information previously unavailable at the molecular level. "Diamond is a million times stiffer than rubber because of its chemical bonds and their organization," Sahin says. "So the hardness of a material is related to its chemical nature. There is no such tool that can tell us hardness at the molecular scale other than what we're building. And by measuring hardness, it is possible to see chemical changes at the surface even at the molecular level."

The improved AFM—and Sahin is working on further modifications to increase resolution even more—should find its first applications in materials science. "We are developing new materials that can really have a big impact on our lives," Sahin notes. "These materials are engineered at the nanoscale. So we need a tool that can go to the nanoscale and tell what



TRADITIONAL atomic-force microscopy (*left*) is less informative than Ozgur Sahin's improved time-resolution AFM. Both images are of a surface consisting of a silicon substrate and two types of polyethylene. The left image shows only general topography. The right image provides specific material content information: silicon is white; ordered polyethylene is light brown; amorphous polyethylene is dark brown.

materials are there, not just their shapes. So this tool will allow people working in that field to see what they're designing." Sahin also foresees biological applications for the new microscope. "It could be a biosensor that enables you to find small amounts of certain molecules. By looking at mechanical changes on a surface, you can determine whether a molecule is or isn't there," he explains.

The Pythagoreans, in their attempts to understand nature, first elucidated the relations between the vibrational frequencies commonly known as musical notes. By exploiting and extending those fundamental relationships, Sahin has created a novel technique for probing deeper into nature. And a certain appreciation for music remains part of his minuscule cantilever, as it bends and sways. "In simulations," Sahin says, "it looks like it's dancing." SA

OZGUR SAHIN

# The Finalists

## Undergraduate Students

Marc Burrell, Rice University: Control system allowing for better CT cardiac scans of patients with pacemakers

Randall Erb, University of Rochester: Ultrasound armband for navigation by blind people

Gillian Hoe, Ashkon Shaahinfar and Elbert Hu, Johns Hopkins University: Instrument for early detection of labor, to prevent premature delivery

Katarzyna Sawicka, Stony Brook University: Biosensor based on polymer-enzyme fibers for early warning of liver or kidney disease

## Graduate Students

**David Berry, Massachusetts Institute of Technology:** Improved targeting of anticancer drugs to tumors, sparing healthy tissue

**Jijumon Chelliserrykattil, University of Texas at Austin:** Creation of stable, modified RNA for potential use in therapeutics

**Pei Yu Chiou and Aaron Ohta, University of California, Los Angeles:** Development of optical, electronic tweezers to maneuver microparticles

**Mohammed El-Salanty, Baylor College of Dentistry:** Device to encourage facial bone growth following trauma or surgery

**Wayne Gellet and Drew Dunwoody, University of Iowa:** New, inexpensive polymer-electrolyte fuel cell

**Benjamin Yellen, Drexel University:** Manufacturing technique based on the magnetic manipulation of microscopic materials

**Sehoon Yoo, Ohio State University:** Process for the creation of microscopic ceramic fibers with industrial uses

# Finals Judges

**Jasemine Chambers,** director of Technology Center 1600, U.S. Patent and Trademark Office's biotechnology branch

**Rose Ann Dabek,** former associate general counsel, Proctor & Gamble

**James Hillier,** inventor of the electron microscope

**Donald B. Keck,** former executive director of research, Corning, Inc.

**Francis Papay,** head of the pediatric plastic surgery section, Cleveland Clinic Foundation

**Stephen L. Squires,** chief science officer, Hewlett-Packard Company

**Gary Wessel,** professor of biology, Brown University

**Woodrow Whitlow, Jr.,** deputy director of the NASA Kennedy Space Center

NOISE-CANCELING HEADPHONES

# Reducing a Roar

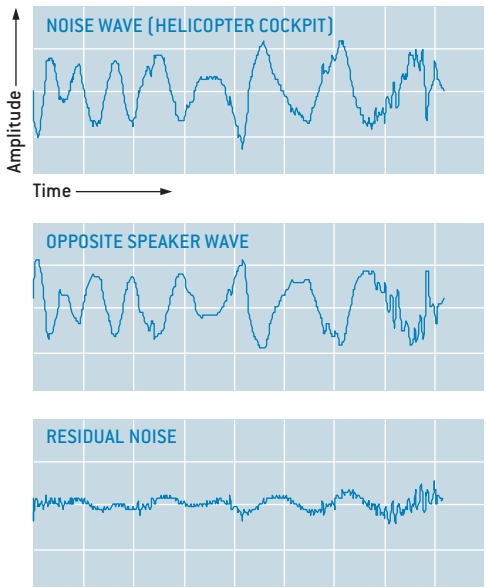
**Whining jet engines** pummel airline passengers with a mind-numbing 75 to 80 decibels of noise. Subways, trains and speeding cars also assail riders with a relentless howl. Putting on simple headphones and cranking up a compact-disc player to drown out the din just adds to the ear-pounding volume.

Deep earplugs or earmuffs like those worn by factory workers typically reduce the racket by 15 to 25 decibels, but they are uncomfortable and do not allow wearers to hear the audio from an airplane movie, music channel or their own music player. Noise-reduction headphones can help. The most advanced models, priced around $300, are made from structural materials that passively block higher-frequency noise (above about 200 hertz). They employ electronics and a speaker to actively cancel lower-frequency sounds, which are otherwise difficult to stop. A microphone inside each muff senses sound waves that make it through the outer ear cup, and a speaker creates pressure waves that cancel them. If desired, music can then be piped in at a comfortable level.

The best models passively reduce noise by 15 to 25 decibels; turning on the active circuitry can cut another 10 to 15 decibels of low-frequency tones. The interior microphone, circuitry and speaker—which constitute a feedback system—must create opposing waves fast and loud enough to almost match the sound in real time. Coming within 25 degrees of the needed 180-degree phase shift can cut noise by 20 decibels. Headphones that react more slowly provide less cancellation.

The electronics can also attack some mid-frequency sounds that seep through, "so the headset can be lighter or less tight, making it more comfortable," says Dan Gauger, noise-reduction research manager at Bose Corporation, a leading maker in Framingham, Mass. But actively attenuating frequencies higher than 500 to 1,000 hertz remains difficult, Gauger explains, because the hardware has less and less time to generate the opposing waves. (For reference, typical female speech is around 225 hertz.) "Feed-forward" systems that pick up noise outside the earpiece and pipe in the opposing signal are also available but require complex electronics. *—Mark Fischetti*

**PRESSURE WAVE** from noise is canceled by destructive interference; the speaker creates a wave that is 180 degrees out of phase and of similar amplitude. Many frequencies are present in the noise.





SAMUEL VELASCO; SOURCE: BOSE CORPORATION

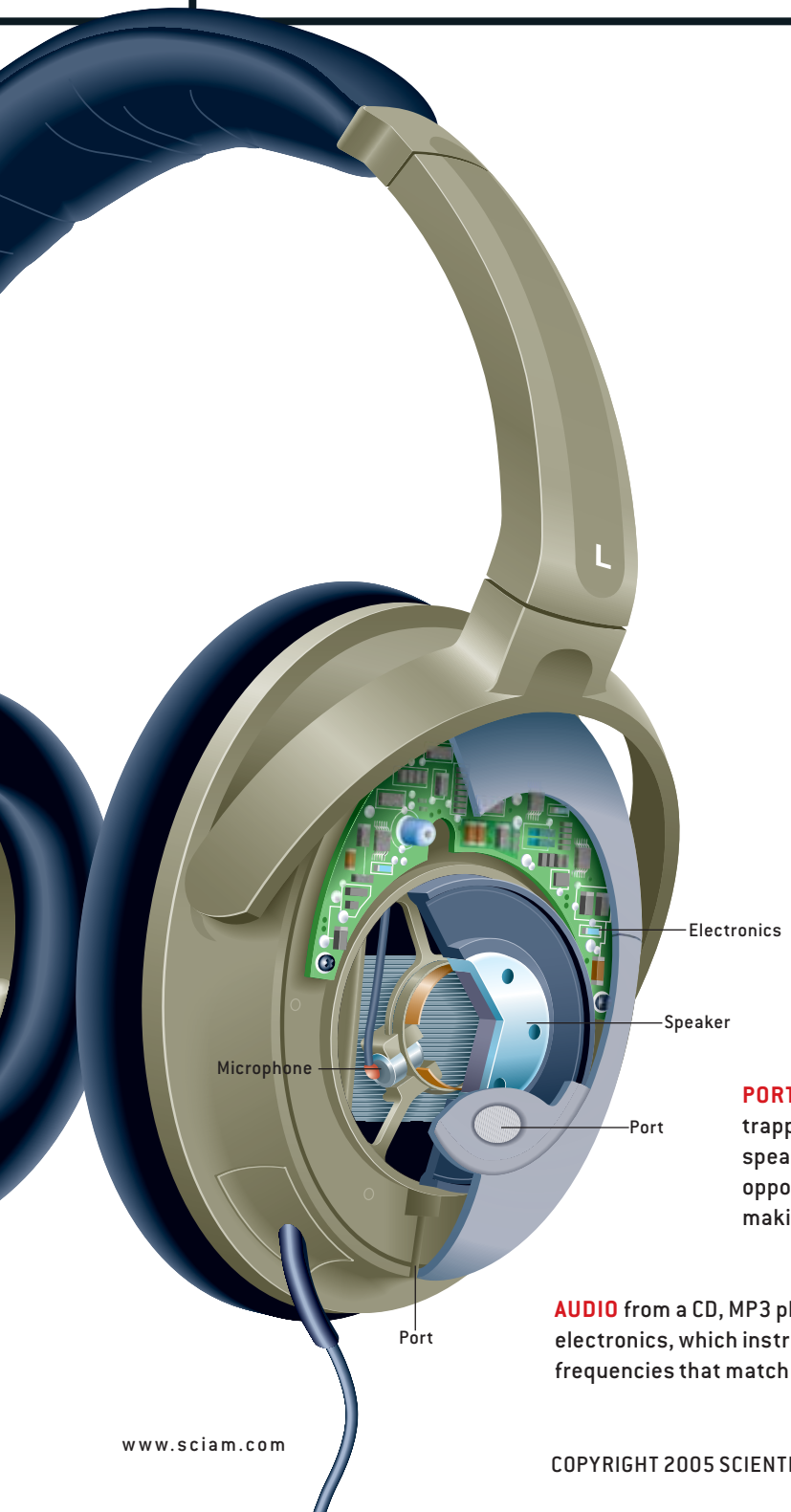
*Have an idea for a topic?*
*Send it to workingknowledge@sciam.com*

## DID YOU KNOW...

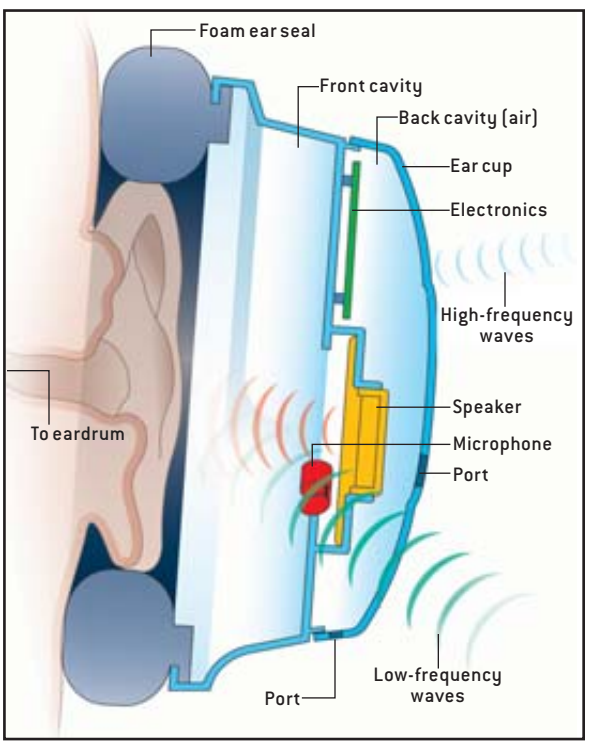
➤ FRAZZLED FLIER: Bose Corporation founder Amar Bose was prompted to craft noise-canceling headphones during an aggravatingly loud plane flight from Europe in 1978. The U.S. Air Force had tried active-cancellation headphones in the 1950s, but invention in the 1970s of the tiny, low-power electret microphone would make possible much lighter gear. Bose worked with air force clients and began selling commercial sets in 1989.

➤ WHAT?!: The National Institute for Occupational Safety and Health says that sustained exposure to sound exceeding 85 decibels can harm human hearing. Scientific studies also indicate that an ongoing roar can magnify fatigue, elevate stress, even prolong jet lag. The decibel scale is logarithmic: 50 decibels is 10 times more powerful than 40 decibels and typically sounds twice as loud. Some average levels: conversation, 50 to 60; inside a four-cylinder car on the highway, 70 to 75; passenger airliner, coach class, 75 to 80; lawn mower, 95; table saw, 105; full-tilt rock concert, 110 to 120.

➤ QUIET COCKPIT: Engineers have attempted to cancel noise in entire cockpits of military aircraft by installing microphones and speakers every few feet all around the interior. Success requires many, often large, speakers, which occupy space and sap power, along with overcoming reverberation and standing waves. Practical systems have achieved quiet zones rather than uniform silence.




**HEADPHONE** ear cup and ear seal attenuate high-frequency sound. Low-frequency noise penetrates, creating pressure waves inside the front cavity. A microphone senses the waves, and electronics direct a speaker to create inverse waves, negating the pressure change before it reaches the eardrum.




**PORTS** increase speaker efficiency by venting air trapped behind it. To cancel a 90-decibel noise, the speaker must be powerful enough to create comparable, opposing sound pressure—an energy-intensive task, making efficiency key.

**AUDIO** from a CD, MP3 player or airplane seat arm is sensed by electronics, which instruct the speaker not to negate noise frequencies that match the desired audio frequencies.

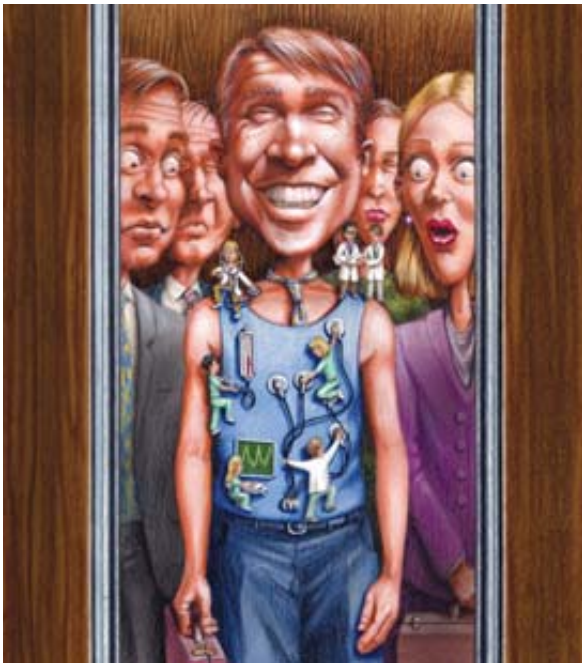
# Every Breath You Take

NOW A HIGH-TECH SHIRT CAN RECORD YOUR VITAL SIGNS ALL DAY AND NIGHT **BY MARK ALPERT**

**I've been a hypochondriac** ever since I was a kid. As an eight-year-old, I was terrified of having a heart attack, and no amount of parental reassurance could erase this fear. In my childish reasoning, these worries seemed perfectly logical—heart attacks were the most common cause of death in my family, and they appeared to strike without much warning. At my most panicky moments in the middle of the night, the only way I could fall asleep was if I kept my hand pressed against my sternum to convince myself that my heart was still beating. When I confessed these anxieties to my father, he tried to point out the ridiculousness of my behavior by suggesting another method of self-diagnosis: "You should also stick a finger in your nose to see if you're still breathing."

My hypochondria has eased a bit over the past 35 years—now I worry more about my kids' health, freaking out over every sniffle and scrape. But I recently discovered that monitoring heart rate and breathing during sleep is not such a ridiculous idea after all. More than 12 million Americans suffer from sleep apnea, a disorder characterized by frequent interruptions of breathing. The cause can be either obstructive—a temporary closing of the soft tissues around the airway—or neurological; in both cases, the condition forces the sleeper to awake briefly to resume breathing, as many as 400 times in a single night. If left untreated, the disorder can raise the risk of cardiovascular problems, but the great majority of sufferers simply endure their nightly struggles and constant fatigue. One obstacle is that doctors cannot definitively diagnose sleep apnea unless the patient spends a night under observation in a sleep lab.

Now a better solution may be at hand. VivoMetrics, a company based in Ventura, Calif., has fashioned a wearable device that can record vital signs throughout the day and night. Called the LifeShirt, it is a sleeveless spandex garment equipped with an electrocardiogram (ECG) for gauging heart rate and embedded wires for measuring respiration. In Denver, a clinic run by Kaiser Permanente is using the LifeShirt to monitor sleep problems in children. "The sleep lab can be a miserable experience for kids," says Elizabeth Gravatte, director of marketing for VivoMetrics. "But they love the LifeShirt. They even brag about wearing it." By examining the data collected by the device, physicians can determine whether a child has sleep apnea and whether the condition is serious enough to warrant a surgical intervention, such as the removal of the tonsils or adenoids.



AMBULATORY CARE: The LifeShirt can monitor your heart rate and breathing without interrupting your daily routine. Developed by VivoMetrics in Ventura, Calif., the device has been used in a variety of medical studies and clinical trials.

JOHN FRASER

The LifeShirt has already proved useful as a tool for medical research. Since the U.S. Food and Drug Administration approved the device in 2002, it has been employed as an ambulatory patient monitor in a variety of studies, ranging from an investigation of coughing in patients with chronic lung diseases to an assessment of stress in subjects with autism. The main advantage of the device is that it can provide researchers with a continuous stream of information about a patient's health. Instead of relying on intermittent tests conducted during office visits, physicians can analyze heart and respiratory rates measured over long periods and use the system's software to pinpoint signs of illness among

the reams of data. Given my lifelong interest in my own vital signs, I was quite intrigued by the LifeShirt. I invited the people from VivoMetrics to come to my office, giving them my chest and abdomen measurements so they could bring along a device that would fit me.

I have to admit, I was a little embarrassed as I donned the LifeShirt in the men's room, pasting the electrodes of the ECG to my chest and squeezing myself into the tight-fitting black spandex. When I emerged, Alex Derchak, director of clinical development for VivoMetrics, explained why the LifeShirt has to fit snugly: the device measures changes in the volume of the rib cage and abdomen by analyzing the frequency of weak oscillating currents flowing through wires embedded in the shirt's elastic bands. A phenomenon called self-induction is at work here: as the current oscillates, the magnetic field around the wire changes, too, inducing voltages that slow the oscillation. The degree of self-induction is proportional to the cross-sectional area of the circuit. As the wearer of the LifeShirt breathes in, the circuit expands and self-induction rises, lowering the frequency of the oscillating current; as the wearer breathes out, the opposite happens.

Derchak connected my LifeShirt to a handheld unit that stores the recorded data on a compact flash memory card. The unit has a touch screen that allows patients to report their symptoms, moods and activities while wearing the LifeShirt. The requested information can vary depending on the type of clinical study. (During sleep studies, the handheld gadget is usually tucked inside a pillow.) The LifeShirt also comes with an accelerometer that can track the wearer's posture and activity level, indicating whether he or she is lying down or standing up, walking or running.

To demonstrate the device's abilities, Derchak suggested that I take a jog down the hallways of the *Scientific American* headquarters. Feeling incredibly foolish, I did three laps through the corridors while my colleagues gaped at me from their offices. "Don't be alarmed!" I called out. "It's all for science!" Derchak gave me a minute to catch my breath and then instructed me to lie down on the floor. (Luckily, he didn't order me to do any push-ups.) After a few more minutes, Derchak popped the flash card out of the handheld unit and inserted it into his laptop so we could review my results.

The laptop's screen displayed an array of squiggly lines. The top line showed my tidal volume—the amount of air inhaled with each breath—over the 16 minutes that I'd worn the LifeShirt. The middle lines detailed my raw ECG data and heart rate, and the bottom lines delineated the jolts of my physical movements. The software allowed us to focus on specific intervals of

the LifeShirt session: when I was talking, when I was running, when I was lying down. I was fascinated to see how my breathing changed when I was speaking—each squiggle elongated as I took a big gulp of air and let it stream out over several seconds. When I was jogging, my heart rate climbed from 93 to 127 beats per minute, and the number of breaths per minute jumped from 19 to 38. And although I was exercising for only a minute and a half, it took more than two minutes for my heart rate to settle back to normal.

The LifeShirt can be outfitted with additional monitoring equipment, including a pulse oximeter for measuring the amount of oxygen in the blood and a throat microphone for determining the frequency of coughing. What is more, VivoMetrics is evaluating other uses for the high-tech garment besides medical research. Fire departments in Connecticut and Minnesota have tested LifeShirts in training exercises; worn under the firefighters' flame-retardant suits, the devices can wirelessly transmit data on heart rate, breathing, blood oxygen level and body temperature to officers in a nearby command truck. And the U.S. Army has signed a contract with VivoMetrics to incorporate the company's technology into a system designed to monitor the vital signs of soldiers during battle.


CHILDREN are especially fond of the LifeShirt. Doctors are using the device to determine if pediatric patients are suffering from sleep apnea, a disorder characterized by frequent interruptions of breathing during the night.

COURTESY OF VIVOMETRICS

But you can't buy your own LifeShirt just yet. VivoMetrics currently leases the garments to clinics and research groups; although the company may eventually offer the LifeShirt to consumers, the plans for retail sales and pricing are still vague. Considering the number of hypochondriacs out there, that's probably just as well. SA

# Big Bang vs. Steady State

HOW THE BIG BANG THEORY WON THE 20TH CENTURY'S BIGGEST COSMOLOGICAL DEBATE **BY CHET RAYMO**


**BIG BANG: THE ORIGIN OF THE UNIVERSE**
by Simon Singh
Fourth Estate (HarperCollins Publishers), 2005 ($26.95)

**When I started teaching** college in 1964, the required reading for my general studies science course included two articles by two prominent physicists published in *Scientific American* eight years previously. George Gamow, a principal architect of the big bang theory, made the case for a universe that began billions of years ago as an explosion from an infinitely dense and infinitely small seed of energy. Fred Hoyle, stalwart champion of the steady state theory, took the stand for an infinite universe with no beginning and no end, in which matter is continuously created in the space between the galaxies.

Both theories explained the outward rush of the galaxies discovered by Vesto Slipher, Edwin Hubble and Milton Humason in the first decades of the century. Both theories had strengths and weaknesses. For example, the big bang successfully accounted for the known abundances of hydrogen and helium in the universe but posited an embarrassing beginning that could not be explained. The steady state theory avoided the stumbling block of a universe that seemed to come from nowhere but replaced it with many little unexplained beginnings (those particles of matter appearing continuously from nothing). Yet the big bang theory made one prediction that was testable: if the universe began in a blaze of luminosity, a degraded remnant of that radiation should still permeate the cosmos, and the precise spectral distribution of this microwave-frequency background could be calculated.

Meanwhile, entirely independently, two radio astronomers at Bell Labs in New Jersey, Robert Wilson and Arno Penzias, were trying to find the source of an annoying hiss in their microwave antenna that seemed to come equally from all parts of the sky. The hiss turned out to have precisely the characteristics predicted by the big bang cosmologists.

For the first time in history, the human mind had constructed a creation story that could be tested empirically. With the discovery of the cosmic microwave background radiation, the big bang delivered a knockout blow to its steady state competitor.

It's a wonderful story, and it deserves a master storyteller. Simon Singh—a physicist with established credentials as a science popularizer—is up to the task. His previous books, *Fermat's Enigma* and *The Code Book*, became international best-sellers. Singh weaves the many threads of the story skillfully together, beginning with the cosmological speculations of the ancient Greeks and ending with the thorny contemporary question, "What came before the big bang?" His tale begins slowly, but only because we know so little about the personal lives of the early players. Singh really gets up to speed as we enter the 20th century, with its lively cast of strong personalities tussling with the universe and with one another.

Two great historical debates lie at the heart of the book. The first concerned whether the spiral nebulae, catalogued throughout the 19th century, are part of our own Milky Way Galaxy, and therefore relatively near, or other "island universes" far away. Resolving this debate meant finding a reliable way to measure the distances to the nebulae. Singh ushers onstage two giants of 20th-century astronomy, Harlow Shapley and Edwin Hubble, who anchored opposite sides of the nebula debate. He also gives star


ATOMIC BOMB muses over the news about the big bang in this cartoon by Herbert L. Block ("Herblock") from 1948. The bomb seems to be calculating how fast it could destroy the world.

COURTESY OF HARPERCOLLINS

turns to astronomers who deserve to be better known, such as Annie Jump Cannon and Henrietta Leavitt. Telescopes played a leading role in the debate, most notably the 100-inch Hooker Telescope on Mount Wilson and the 200-inch Hale reflector on Mount Palomar, both in California. These instruments enabled astronomers to resolve the nebulae into stars, which provided the necessary distance indicators.

The spiral nebulae are indeed other Milky Ways. Once the nebula debate was resolved, Hubble recognized the expansion of the universe, and a second great debate came to the fore: big bang vs. steady state. Big ideas and big egos were at stake. Gamow and Hoyle, in particular, squared off against each other, even in the pages of this magazine.

Then came the discovery of the cosmic background radiation in the mid-1960s by the Bell Labs radio astronomers. No sooner had I introduced my students to the most contentious cosmological debate of the 20th century than the universe whispered the resolution.

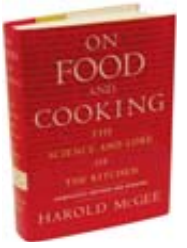
Singh spins out the drama with verve and wit. We meet scientists who are shy and retiring and others with a flair for contention, epic discoveries made serendipitously and beautiful theories shot down by intractable facts, a pooch named Kepler and a persistent pigeon that made its home in the Bell Labs telescope. This is a perfect book for anyone who wants to know what science is all about. SA

*Chet Raymo has taught physics at Stonehill College and written about science for the* Boston Globe. *His latest book is* Climbing Brandon: Science and Faith on Ireland's Holy Mountain. *He resides on the web at www.sciencemusings.com*

## THE EDITORS **RECOMMEND**

### ON FOOD AND COOKING: THE SCIENCE AND LORE OF THE KITCHEN

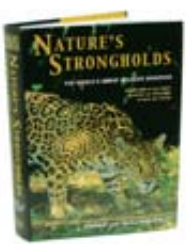
***by Harold McGee. Completely revised and updated. Scribner, 2004 ($35)***




"In 1984, canola oil and the computer mouse and compact disc were all novelties… [and] the worlds of science and cooking were neatly compartmentalized." A lot has changed in 20 years: magazines and books now discuss the science of cooking, and culinary schools offer "experimental" courses that investigate the whys of cooking. So McGee, a writer who specializes in the chemistry of food and cooking, has completely rewritten his 1984 classic, expanding it by two thirds into a book that weighs in at almost 900 pages. He offers thorough, scientific explanations of countless topics, including why brining your turkey is not a good idea, why food wrapped in plastic often tastes like plastic, why you should never refrigerate tomatoes. And he continues to display, as one admirer said of the first edition, "a scientist's skill and a cook's heart."

### NATURE'S STRONGHOLDS: THE WORLD'S GREAT WILDLIFE RESERVES

***by Laura and William Riley. Princeton University Press, 2005 ($49.50)***




From Botswana to the Camargue, from Denali to Komodo Island, this book covers more than 600 reserves in over 80 countries. The authors, long-time nature writers and conservationists, have included information on how to visit these extraordinary sites, their ecological significance and some historical background. Most of the world's charismatic and endangered species—many depicted here in gorgeous color photographs—owe their continued existence to such reserves, the last places on earth where nature remains more or less intact. The volume itself is a terrific resource.

### JOHN JAMES AUDUBON: THE MAKING OF AN AMERICAN

***by Richard Rhodes. Alfred A. Knopf, 2004 ($30)***


"The sharp cries of gulls wheeling above the East River docks welcomed the handsome young Frenchman to America." Born in 1785 the illegitimate son of a French planter on Saint Domingue (now Haiti) and raised in France, the handsome young man transformed himself into the consummate American. Rhodes, Pulitzer Prize–winning author of *The Making of the Atomic Bomb,* traces this journey with insight ("studying birds was how he mastered the world, and himself") and vivid language. In particular, Audubon's wife, Lucy—a beautiful, adventurous Englishwoman whom he met shortly after arriving in America—emerges as a full, and patient, partner in Audubon's single-minded enterprise to develop a technique that would breathe life back into the birds he drew and to catalogue the birds of North America in a "collection not only valuable to the scientific class, but pleasing to every person." The book includes several color reproductions to remind us just how well Audubon succeeded.

If this biography inspires you to read more about birds, two other recent books stand out: ***The Race to Save the Lord God Bird,*** by Phillip Hoose (Melanie Kroupa Books, Farrar, Straus and Giroux, 2004, $20), and ***On the Wing: To the Edge of the Earth with the Peregrine Falcon,*** by Alan Tennant (Alfred A. Knopf, 2004, $26.95).

*The books reviewed are available for purchase through www.sciam.com*

# Sticker Shock

IN THE BEGINNING WAS THE CAUTIONARY ADVISORY **BY STEVE MIRSKY**

**Brushfires are raging** all across America over the teaching of evolution, as various antievolution interests attempt to give religiously based views equal footing in science classes. These fires are fueled by so-called creation scientists, who allege that they have scientific evidence against evolution. (They don't.) Their co-conspirators, the "intelligent design" crowd, go with the full-blown intellectual surrender strategy—they say that life on earth is so complex that the only way to explain it is through the intercession of an intelligent superbeing. (They don't mention you-know-who by name as the designer, but you know who you-know-who is, and it isn't Brahma.)

One little blaze can be found in Cobb County, Ga. As this issue of *Scientific American* went to press, a federal judge in Atlanta was in the process of deciding whether biology textbooks in the county could continue to sport a warning sticker that read: "This textbook contains material on evolution. Evolution is a theory, not a fact, regarding the origin of living things. This material should be approached with an open mind, studied carefully, and critically considered."

Maybe that last sentence should be stamped into *every* textbook (and some other books I can think of). And maybe they could rewrite the advisory so that it's accurate. Perhaps something like, "Variation coupled with natural selection is the most widely accepted theory that explains evolution. Evidence for evolution itself is so overwhelming that those who deny its reality can do so only through nonscientific arguments. They have every right to hold such views. They just can't teach them as science in this science class."

But why pick on evolution in the first place when there's so much to be offended by in virtually any science class? I propose that Cobb County–style stickers be placed in numerous other textbooks. Here are some suggestions:


Sticker in *Introduction to Cosmology:* "Astronomers estimate the age of the universe to be approximately 13 billion years. If evolution ticks you off because you believe that the earth is only 6,000 years old, cosmology should really make smoke come out of your ears. There's a fire extinguisher next to the telescope."

Sticker in *Geography for Today:* "Some people believe that the earth is flat. An ant probably thinks the beach ball he's walking on is flat, too. Anyway, this book says the earth is more like an oblate spheroid. Now go find Moldova on a map."

Sticker in *Earth Science:* "You are free to exercise your First Amendment rights in this class and to identify all stratigraphic layers as being 6,000 years old. We are free to flunk you."

Sticker in *Collegiate Chemistry:* "Electrons. They're like little tiny ball bearings that fly around the atomic nucleus like planets orbit the sun. Except that they're actually waves. Only what they really are are probability waves. But they do make your MP3 player run, seriously."

Sticker in *Our Solar System:* "Remember they said in chemistry class that electrons fly around the nucleus like planets orbit the sun? Some people think the sun and other planets go around the earth. You'll have a much easier time with the math if you just let everybody go around the sun, *trust* me."

Sticker in *Physics for Freshmen:* "We know that a lot of what's in this book is wrong, and with any luck they'll eventually find out that even more of it is wrong. But it's not so far off, it took some real geniuses to get us this close, and it's way better than nothing."

Sticker in *Creationism for Dummies:* "Religious belief rests on a foundation of faith. Seeking empirical evidence for support of one's faith-based beliefs therefore could be considered pointless. Or even blasphemous."

Sticker in *Modern Optics:* "CAUTION! Dark ages in mirror may be closer than they appear." SA

ILLUSTRATION BY MATT COLLINS; PHOTOGRAPH BY FRANK VERONSKY

# ASK THE EXPERTS

## Q Why do bags form below our eyes?

—K. Davin, Juneau, Alaska

**Rhoda S. Narins, clinical professor of dermatology at New York University Medical Center and president of the American Society for Dermatologic Surgery, explains:**

Dark circles and bags under the eye occur for several reasons: the skin there is much thinner than it is elsewhere on the body and becomes looser as we age. This very thin skin also sits on top of underlying purple muscle and blood vessels and therefore appears darker. In addition, some people have hereditary pigmentation in this area. As we age, fat comes out of the space enclosed by the eye socket, called the orbit, and forms a puffy area under the eye. This fatty tissue can fill with water, making the hollow appear even deeper. The condition becomes even more noticeable when water is retained in the fat pad, which can occur for a variety of reasons, including eating too much salt, lying flat in bed, not getting enough sleep, allergies and monthly hormonal changes.

Treating the hollow space under the eye is straightforward and can be done by injecting a filler such as Restylane. Immediately after this procedure, the so-called tear trough is softened, and any visible pigmentation becomes noticeably lightened. A carbon dioxide ($CO_2$) laser also can be used to resurface the skin, which tightens and thickens it as well as lightening the coloring. For hereditary pigmentation, $CO_2$ laser resurfacing and bleaching creams are sometimes helpful. As an option, a surgeon can perform blepharoplasty to fix the fat pad under the eye.

Simple, nonsurgical measures to reduce the puffiness and darkness of under-eye circles include avoiding salt, using cold compresses on the eyes, getting enough sleep, treating allergies, as well as sleeping with your noggin higher by resting it on two pillows or raising the head of the bed.

## Q How are the abbreviations of the periodic table determined?

**Michael R. Topp, professor of chemistry at the University of Pennsylvania, offers this answer:**

Although some of the symbols in the periodic table may seem strange, they all make sense given a little background information. For example, the symbol for the element mercury, Hg, comes from the Latin word *hydrargyrum,* meaning "liquid silver." Many other elements that were known to the ancients also have names derived from Latin.

The rare (or inert) gases were discovered more recently and tend to have classical-sounding names based on Greek. For example, xenon (Xe) means "the stranger" in Greek and argon (Ar) means "inert." Helium (He) is named after the Greek god of the sun, "Helios."

So far 110 elements have been formally named. The "new" elements are synthetic, and each one's detection needs confirmation. After the finding is confirmed, the discoverers may propose a name, and then the moniker is officially determined jointly by the International Union of Pure and Applied Chemistry (IUPAC) and the International Union of Pure and Applied Physics (IUPAP).

The proposal to name element 111 roentgenium (Rg), for instance, has been recommended for approval by the Inorganic Chemistry Division Committee of IUPAC. As it states: "This proposal lies within the long-established tradition of naming elements to honor famous scientists. Wilhelm Conrad Roentgen discovered x-rays in 1895."

As yet undiscovered elements with higher atomic numbers receive so-called placeholder names, which are simply Latinized versions of their atomic numbers. Thus, element 111 was formerly designated unununium, literally "one one one" (Uuu), and element 112 has been given the temporary name of ununbium (Uub). SA

*For a complete text of these and other answers from scientists in diverse fields, visit www.sciam.com/askexpert*

MATT COLLINS