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# SCIENTIFIC AMERICAN

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How to Build **NANOTECH MOTORS**

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## WHAT MAKES US HUMAN?

What tiny genetic changes say about our evolution

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How Planets Lose Their Atmospheres

# FEATURES

SCIENTIFIC AMERICAN May 2009 ▪ Volume 300 Number 5








### ON THE COVER

We share nearly 99 percent of our DNA with chimps, yet we differ profoundly. Insights into changes in the human genome reveal why. Photographs by Cary Wolinsky.

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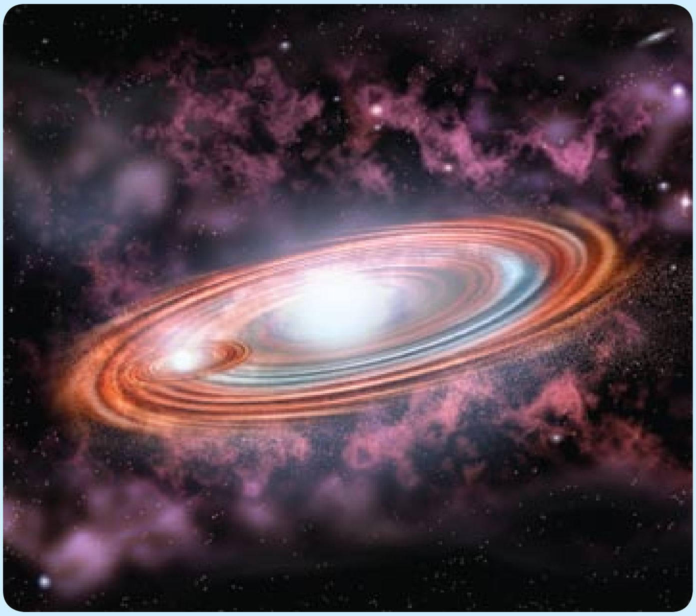

P. MARENFELD *National Optical Astronomy Observatory/Association of Universities for Research in Astronomy/National Science Foundation*

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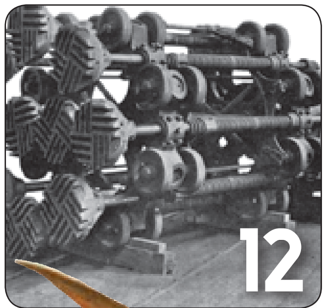
# DEPARTMENTS

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JOE TUCCIARONE *Photo Researchers, Inc.*



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# See No Evil?

**Primates can be dangerously harmful, especially the human ones**

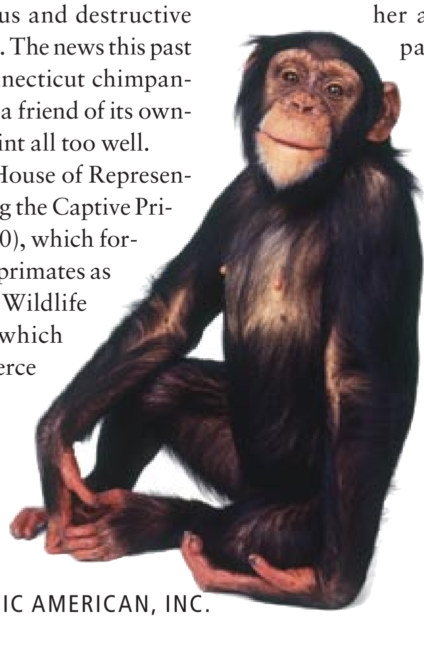
**Tarzan had a chimpanzee, Chee**ta, in the movies and a monkey, Nikima, in the source novels. Of course, Tarzan had been raised by apes, and he lived in a jungle, so perhaps his pets were a special case. Then again, Clint Eastwood made a pair of movies about a California trucker with an orangutan, Clyde. On television's *Friends,* the hapless Ross owned a spider monkey named Marcel for a season or so. The Man with the Yellow Hat had his hands full with Curious George, but nothing seriously bad ever happened. Why, then, has my wife so consistently vetoed my frequent suggestion that we buy a pet monkey to dress as a cowboy and ride on our dog's back as a tourist attraction in Central Park? What does she have against monkeys?

Needless to say, my wife is right (and for the record, I was joking). In fiction, apes and monkeys are portrayed as clever, charming companions that are at worst mischievous and at best capable of stealing keys from your captor to unlock the cell where you are being imprisoned. The reality is far less fun: not only do they resist housebreaking and become sick easily, but their propensities for jealousy and misunderstanding human body language can make them turn vicious and destructive with very little warning. The news this past February about a Connecticut chimpanzee's horrific attack on a friend of its owner underscored that point all too well.

Cheers to the U.S. House of Representatives, then, for passing the Captive Primate Safety Act (HR 80), which forbids interstate trade in primates as pets. Like the Captive Wildlife Safety Act of 2003, which banned similar commerce in lions and other big, undomesticated cats, the primate bill targets only the use of the animals as pets, making exemptions for research, zoos and even helper monkeys trained to assist the disabled. A version of this smart legislation is moving to the Senate as I write this, and I hope that it passes.

A criticism raised against the Captive Primate Safety Act was that monkey attacks hardly constitute a burning threat to the nation. True, but restricting the sale of monkeys and apes would not just protect humans from their hairier cousins, but also vice versa. Keeping these creatures as pets is fundamentally cruel. They are neither little people nor dogs nor something in between, and they do not prosper if kept in the human world. Without anthropomorphizing them, we should mind their capacity to suffer. Indeed, although I personally still accept the use of primates in laboratories as often justifiable, the mounting evidence for their high intelligence and awareness increasingly challenges my confidence in the ethics of that position.

The record of our evolutionary separation from other primates can be read in a comparison of human and chimpanzee DNA, as Katherine S. Pollard discusses in her article, beginning on page 44. Discover the astonishingly small changes in the genome that distinguish Tarzan from Cheeta. And if you are in the market for an extremely small cowboy costume, I can offer you a bargain. ■



**JOHN RENNIE**
*editor in chief*

FLYNN LARSEN (*Rennie*); DORLING KINDERSLEY *Getty Images (chimp)*; COURTESY OF DAVID C. CATLING (*Catling*)

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**DAVID C. CATLING** is a member of the University of Washington faculty and a co-investigator for NASA's Phoenix lander project, which studied the surface of Mars.

**THOMAS E. MALLOUK** is professor of materials chemistry and physics at Pennsylvania State University, where his work focuses on nanoscale inorganic materials.

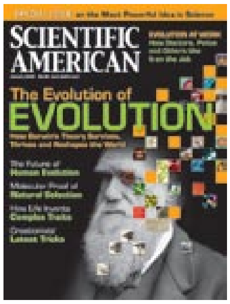
**KATHERINE S. POLLARD** is a biostatistician at the University of California, San Francisco. She recently began studying the evolution of microbes that live in the human body.

**AYUSMAN SEN** is a Penn State professor of chemistry and collaborated with Mallouk on developing the idea for a nanoscale motor powered by a catalytic reaction.

editors@SciAm.com



# Creationism ■ NASA Budget ■ Evolutionary Psychology




JANUARY 2009

**"The questions students should ask are, Does intelligent design make predictions? And can those predictions be tested?"**
*—Oscar Estévez*
UNIVERSITY OF AMSTERDAM MEDICAL CENTER

## ■ Creationist Controversy

"The Latest Face of Creationism," by Glenn Branch and Eugenie C. Scott, details the tactics of those agitating against the teaching of evolution in public schools. Scientists have, to some extent, contributed to creationists' arguments by using the term "theory" when referring to evolution. It is not a theory but an established law.

Robin A. Cox
Scarborough, Ontario

Simply suppressing the teaching of intelligent design (ID) sends the wrong message to students. They ought to learn that science is about understanding the world and that it proceeds in stages. The questions they should ask are, Does ID make predictions? And can those predictions be tested? If the answers to both are negative, they themselves can conclude that ID is "only a nonscientific theory."

Oscar Estévez
Emeritus Professor of Medical Informatics
University of Amsterdam Medical Center

## ■ Budgeting Space

George Musser's "Space Sticker Shock" [News Scan] cites the challenges of developing cutting-edge NASA missions within fiscal bounds. In recent years NASA has thoroughly reviewed and updated our approach to grappling with uncertain cost projections for first-of-a-kind missions.

NASA commits only to a cost and schedule after completing a detailed study that ascertains technological readiness, manufacturing capabilities and funding availability. In cases such as the James Webb Space Telescope (JWST), a thorough technology evaluation phase was first required. NASA committed to $1.6 billion in 2006 for the Mars Science Laboratory (MSL) and plans to make a commitment for the JWST in early 2009. The National Academy of Sciences's decadal survey cost numbers for those projects that Musser quotes never represented NASA's commitment.

When we commit to a mission in a confirmation review, we strive to develop it within its approved budget. We are also working constructively with the next decadal surveys to improve early cost estimates for new initiatives.

Jon Morse
Director, NASA Astrophysics Division
James Green
Director, NASA Planetary Science Division

Read an extended version of this letter at **www.SciAm.com/sticker**

## ■ Pop Psychology Probe

In "Four Fallacies of Pop Evolutionary Psychology," David J. Buller tries to dismiss evolutionary psychology (EP) as "pop" science. Yet all thriving sciences are (and should be) popularized. The *primary* research in EP has been published in leading scientific journals and has garnered top scientific prizes. Buller errs in claiming that EP's main goal is to identify *when* psychological mechanisms evolved (it is to characterize their function), that it attributes all adaptation to Pleistocene conditions (this is an empirical, not an a priori, question) and that adaptation can only be demonstrated by phylogenetic comparison (it hinges on the fit between predictions from optimality analyses and data from genetics, experimentation, ethnography and social science databases).

His accusation that EP is "speculative" has long been refuted (in the November 2003 *Psychological Bulletin*, one of us documented over 50 empirically supported novel predictions), as has his claim that topics such as sexual jealousy are only studied with questionnaires (methods range from psychophysiology, neuroimaging and reaction time to ethnography and divorce records). All scientific endeavors should be subject to criticism, but Buller's polemic manufactures misinformation.

David M. Buss
University of Texas at Austin
Steven Pinker
Harvard University

FRANK STOCKTON

**CRITICS of a major branch of evolutionary psychology question whether we can know our Stone Age ancestors' psychology.**

BULLER REPLIES: *Buss and Pinker credit me with too much originality. For the most part, I have simply synthesized criticisms of EP made by numerous biologists, anthropologists and psychologists. I discuss those criticisms in my book* Adapting Minds *(MIT Press, 2005), which also addresses EP's primary research. Moreover, I've never made the strong claims they attribute to me (for example, about "EP's main goal" and that jealousy is "studied solely with questionnaires"). That is misinformation. Finally, publication in "leading journals" and receipt of "top prizes" are not hallmarks of truth. Half a century ago the behaviorist paradigm could have been similarly defended. Yet today the majority of psychologists agree that it was fundamentally misguided. Skeptics like me merely suspect that 50 years from now the current EP program will appear much the same.*

## Funding Flap

In "Flies and Projectors and Bears, Oh My" [Anti Gravity], Steve Mirsky ridicules Senator John McCain and Governor Sarah Palin for criticizing federal funding for specific scientific projects. Mirsky must not believe that those who benefit from research should pay for it. He notes that the fruit-fly research Palin cited would benefit olive growers in California. So why, then, shouldn't California and the growers be responsible for the funding? And Illinois should pay for its planetarium's projector. Research at the public's cost is not an entitlement but a subject open to debate.

J. J. Marinello
West Hartford, Conn.

MIRSKY REPLIES: *I could have considered McCain's and Palin's attacks on federal funding as opportunities to mull over whether the projects were prudent uses of federal money. But that wasn't the criticism the candidates offered: they clearly argued that the projects were self-evidently ridiculous, as Louisiana Governor Bobby Jindal did by ridiculing "something called volcano monitoring" in his reply to President Barack Obama's speech before a joint session of Congress. This apparently deep-rooted disrespect for science is counterproductive.*

**ERRATA** In "Testing Natural Selection," by H. Allen Orr, the box "What's Good for the Group," by Steve Mirsky, gives the wrong affiliation for Richard Dawkins. Dawkins is at the University of Oxford.

"Evolution in the Everyday World," by David P. Mindell, reports incorrect habitats for the two African elephant species. *Loxodonta Africana* lives primarily in the savanna and *L. cyclotis* in the forest.

"Playing Chicken," by David Biello [News Scan], should have stated that farmed chickens lack 50 percent of their genome's genetic diversity, not its genes.

## Letters to the Editor

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# 50, 100 & 150 YEARS AGO

Innovation and discovery as chronicled in Scientific American

## Eye and Spectrum ■ Calling Mars ■ Ratwear

*Compiled by Daniel C. Schlenoff*

### MAY 1959

**THE COLOR OF LIGHT**—"No student of color vision can fail to be awed by the sensitive discernment with which the eye responds to the variety of stimuli it receives. Recently my colleagues and I have learned that this mechanism is far more wonderful than had been thought. The eye makes distinctions of amazing subtlety. It does not need nearly so much information as actually flows to it from the everyday world. It can build colored worlds of its own out of informative materials that have always been supposed to be inherently drab and colorless. —Edwin H. Land" [founder of Polaroid Corporation]

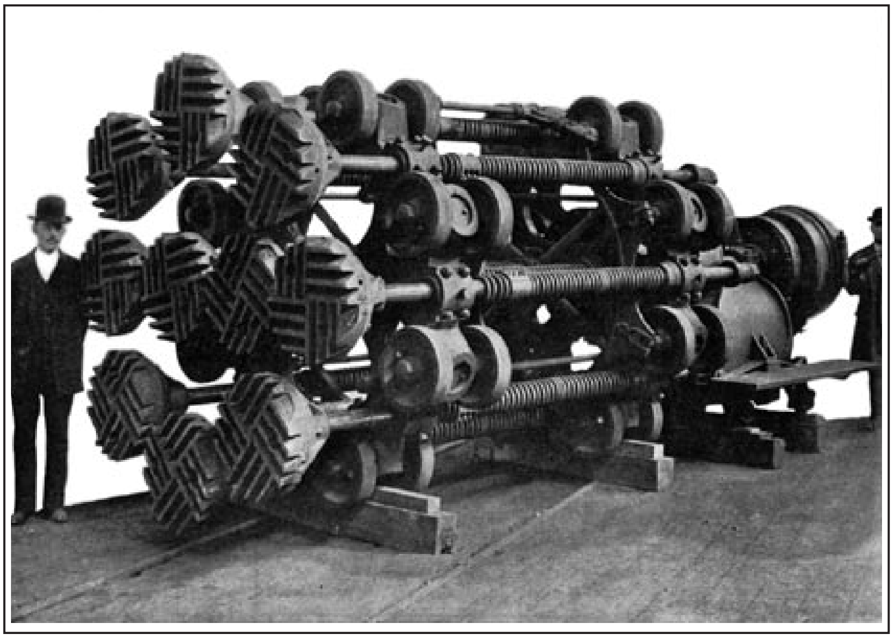
**"CARGO CULT" ANTHROPOLOGY**—"In the central highlands of New Guinea the sudden transition from the society of the stone ax to the society of sailing ships (and now of airplanes) has not been easy to make. As the agents of the Australian Government penetrate into ever more remote mountain valleys, they find these backwaters of antiquity already deeply disturbed by contact with the ideas and artifacts of European civilization. For 'cargo'—Pidgin English for trade goods—has long flowed along the indigenous channels of communications from the seacoast into the wilderness. These people are only the latest to be gripped in the recurrent religious frenzy of the 'cargo cults.' These cults, however variously embellished with details from native myth and Christian belief, all advance the same central theme: the world is about to end in a terrible cataclysm. Thereafter God, the ancestors or some local culture hero will appear and inaugurate a blissful paradise on Earth."

The entire article from 1959 is available at **www.SciAm.com/may2009**

### MAY 1909

**POWER DIGGER**—"Like the poor, new ideas for tunneling through rock and doing away with drilling and powder and dangerous blasting are forever with us. Since 1853 there have been no less than sixty-nine patents granted on tunneling machines. The one shown in the photograph was constructed in the East and shipped to Georgetown, Colo. Ready for work, it weighs 29 tons. Its huge frame holds ten monster crushing heads. The machine works on the principle of pulverizing the rock instead of cutting it. It is claimed that if each head penetrates but the thickness of a sheet of paper with each blow, it will cut at the rate of an inch a minute."

**E.T., MIRROR HOME**—"Much excitement has been created by Prof. Pickering's proposal to build a system of mirrors, by means of which light can be rhythmically flashed to Mars. According to Prof. Pickering, a system of reflecting surfaces of adequate area could be constructed at a cost of $10,000,000. Would it be worth while to carry out the idea? If an answering signal should be received, it would be safe to say that the event would transcend in interest and importance the most stirring occurrence in the history of the earth, and would inaugurate a new era in the progress of the human race. Even in the face of this tremendously alluring, but exceedingly remote possibility, it seems to us that the $10,000,000 could be more worthily expended elsewhere."



**TUNNELING MACHINE** for bashing a way through solid rock, 1909

SCIENTIFIC AMERICAN, VOL. C, NO. 21; MAY 22, 1909

### MAY 1859

**RECESSION LUXURY?**—"An ingenious individual, of Liskeard, Cornwall, England, has, for some time past, been exhibiting himself in a dress composed from top to toe of rat-skins, which he has been collecting for three years and a half. The dress was made entirely by himself; it consists of hat, neckerchief, coat, waistcoat, trousers, tippet, gaiters, and shoes. The number of rats required to complete the suit was six hundred and seventy; and the individual, when thus dressed, appears exactly like that of the Esquimaux described in the travels of Parry and Ross."

# Mass Extinctions ▪ Stem Cell Ban Lifted ▪ Universal Flu Vaccine ▪ Free to Sue

*Edited by Philip Yam*

## Permian Puzzle

The mass extinction at the end of the Permian period 250 million years ago wiped out at least 90 percent of all ocean species and 70 percent of land vertebrates [see "The Mother of Mass Extinctions"; SciAm, July 1996]. New findings suggest the deadly event on land might have occurred separately from the one in the oceans.

Paleontologist Robert Gastaldo of Colby College and his colleagues investigated ancient sedimentary rock at South Africa's Karoo Basin. Previous expeditions there had identified a distinct boundary between the Permian and the Triassic, which came right after. Dubbed the "lifeless zone," this sediment lies over fossils of extinct reptiles and has been the primary evidence of the end-Permian extinction's rapid effects on land.

**FOSSIL of a Permian amphibian that was the first vertebrate to conquer land but died out in a mass extinction.**

But now Gastaldo's team has discovered that some of the sediment lies roughly eight meters below the Permian-Triassic boundary—and at some places it lies below those fossils, meaning it was deposited well before the catastrophe was thought to have happened on land. The change in timing suggests that the land and marine extinctions could have had different triggers. Culprits that could have altered the climate and oceans in a deadly way include sustained volcanism and continental drift. Dig into the March *Geology* for more. —*Charles Q. Choi*

## Restrictions Removed

As expected, President Barack Obama signed an executive order on March 9 lifting a ban on stem cell research imposed by the Bush administration in 2001. That restriction had limited scientists who received federal funding to 21 lines of embryonic stem cells, possibly hampering efforts to transform the cells into therapies [see "The Future of Stem Cells"; SciAm, July 2005]. Now investigators can use hundreds of new lines, and some of the $10 billion in the economic stimulus package for health care research will likely flow into embryonic stem cell work. The Department of Health and Human Services will issue ethical and reporting guidelines this summer.

## Clue against Flu

A goal in fighting influenza is a universal vaccine, one that works on many strains of the pathogen [see "Beating the Flu in a Single Shot"; SciAm, June 2008]. But the virus's outer coat, consisting mainly of proteins called hemagglutinin and neuraminidase, frequently mutate, forcing the reformulation of vaccines every season. Two studies report the discovery of human antibodies that target an area on hemagglutinin that does not change much. (In contrast, current drugs, such as Tamiflu, aim for neuraminidase.) In tests, one of the antibodies protected mice from lethal doses of avian flu (H5N1) and other strains. Large amounts were needed, however, so any human treatment could be expensive. The papers were published in the March *Nature Structural and Molecular Biology* and online February 26 by *Science Express*.

**NEW HOPE for a one-time flu shot.**

## Legal Side Effects

Drug companies have been left wide open for lawsuits by a March 4 U.S. Supreme Court decision allowing juries to award damages for harmful side effects, even if the drug had proper, FDA-approved warning labels. This ruling, against Wyeth Pharmaceuticals, may encourage more settlements, such as those for Merck's painkiller Vioxx, which triggered heart attacks in some patients [see "Doubt Is Their Product"; SciAm, June 2005]. It could also provide impetus for new legislation to permit lawsuits against medical device makers, which the court shielded from suits last year. —*Kate Wilcox*

SHEILA TERRY *Photo Researchers, Inc. (fossil)*; CHRIS KLEPONIS *Getty Images (Obama signing)*; JEFF HAYNES *Getty Images (flu shot)*

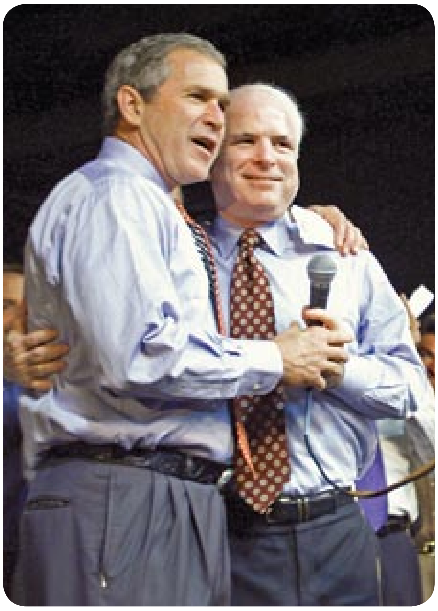
BEHAVIOR

## Taming the Urge to War

**Must lethal conflict be an inevitable part of human culture?** BY JOHN HORGAN

SALT LAKE CITY—As deep as scientists peer into human history and prehistory, they have found evidence of violence. That was the bad news from 17 researchers in anthropology and other fields at "The Evolution of Human Aggression: Lessons for Today's Conflicts" conference, held at the University of Utah at the end of February. The good news is that much can be done to reduce lethal conflict in the world today. As participant Frans B. M. de Waal of Emory University put it, humans are not "destined to wage war forever."

De Waal, who studies primates, noted that observations of lethal group encounters among chimpanzees, our closest genetic relatives, have promulgated the fatalistic belief that "war is in our DNA." But chimps are also "peacemakers," de Waal pointed out; they reconcile after fights by hugging, mouth and hand kissing, mutual grooming and food sharing. Humans engage in such behavior, too, de Waal said, flashing a photograph of John McCain and George W. Bush embracing—albeit with hideously insincere grins—after their bitter primary contest in 2000.



BURYING THE HATCHET **with a hug is common among primates who need to keep a working relationship after a fight, be it by chimpanzees after, say, a quarrel over food or George W. Bush and John McCain after their bitter primary battle in the 2000 presidential race.**

KARL AMMANN *Getty Images (chimps)*; PAUL BUCK *Getty Images (Bush and McCain)*

Reconciliation takes place, de Waal contended, "whenever parties stand to lose if their relationship deteriorates." Chimpanzees from different troops, which compete for territory and hence treat one another with lethal hostility, rarely if ever reconcile, he noted. Among humans, however, "interdependencies between groups or nations are not unusual." To promote peace, he suggested, nations should foster economic interdependence through alliances such as the European Union. Although the E.U. has "not created love between Germany and France" and other former adversaries, de Waal acknowledged, it has greatly reduced the likelihood of war in Europe.

Harvard University anthropologist Richard Wrangham agreed with de Waal that primate violence is not compulsive, or "instinctual," but is "extremely sensitive to context." One of the most robust predictors of violence between two groups of primates, Wrangham proposed, is an imbalance of power. Chimps from one troop invariably attack individuals from a rival troop when the attackers have an overwhelming number advantage and hence a minimal risk of death or injury.

Although humans are much less risk-averse than chimps, Wrangham asserted, human societies—from hunter-gatherers to modern nations such as the U.S.—also behave much more aggressively toward rival groups when they are confident they can prevail. Reducing imbalances of power between nations, Wrangham said, should reduce the risk of war.

So should controlling population, according to anthropologist Polly Wiessner of the University of Utah. Wiessner is an authority on the Enga, a tribal people who raise crops and pigs in the highlands of Papua New Guinea. Warfare first surged among them 200 years ago, Wiessner said, after the introduction of sweet potatoes led to food surpluses and rapid population growth. Mortality rates subsided after Enga elders instituted stricter rules for warfare, such as bans on killing of women and mutilation.

The introduction of modern medicine into Enga society some 25 years ago decreased childhood mortality, triggering another "youth bulge" and surge in tribal conflict. Mortality rates have soared, Wiessner explained, because Engans now fight with shotguns and automatic weapons rather than clubs, knives and spears, their traditional weapons. Moreover, young mercenaries called "Rambos" hire themselves out to tribes in exchange for cash, young women and other booty. Together with promoting birth control, giving young men "a meaningful way forward in life" should decrease violence, Wiessner proposed.

Climate change has also driven conflict. This lesson emerged from Patricia Lambert's studies of the Chumash, hunter-gatherers who inhabited the coast of southern California for millennia before the arrival of Europeans. Many Chumash skeletons display signs of violence, including skull fractures and embedded arrow or spear points. Analysis of tree rings and other evidence, said Lambert, an anthropologist at Utah State University, suggest that violence among the Chumash escalated during periods of drought.

Lambert warned that droughts, which are expected to increase as a result of global warming, are already triggering conflicts around the world today. To drive this point home, she flashed a photograph of a well in Somalia; so far 250 Somalians have died battling over control of the well. To forestall such conflicts, Lambert said, governments must ensure equitable distribution of water and other resources.

The most upbeat speaker was Harvard psychologist Steven Pinker, who argued that—contrary to what many scientists once believed—levels of violence are much lower in our era than they were before the advent of modern states some 10,000 years ago. According to ethnographic surveys and archaeological evidence, Pinker pointed out, 30 percent or more of the members of tribal societies died as a result of group violence; that percentage is some 10 times greater than the proportion of Europeans and North Americans killed by war-related causes during the cataclysmic 20th century.

Pinker identified several possible reasons for this trend. First, our increased life expectancies make us less willing to risk our lives by engaging in violence. Second, the creation of stable governments with effective legal systems and police forces has eliminated what British philosopher Thomas Hobbes called the "war of all against all" among pre-state humans. Third, mass media and travel have boosted understanding of, and empathy toward, those beyond our immediate family and even nation. This may be the best news of all: civilization, which has often been blamed for war, is actually helping us achieve peace.

*John Horgan is director of the Center for Science Writings at the Stevens Institute of Technology.*

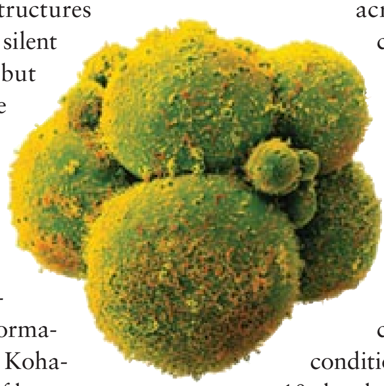
ONCOLOGY

# Primal Programs

**Rethinking cancer by seeing tumors as a cellular pregnancy** BY CHRISTINE SOARES

One reason cancer is not considered a single disease but many is that every cancer cell seems to be dysfunctional in its own way. Random mutations in a cell's DNA initiate its slide into abnormal behavior. And as additional mutations accumulate, that randomness is also thought to account for the diversity in different patients' tumors, even when they are cancers of the same tissue. But evidence is growing that there is a method to the madness of tumor cells, making some scientists reevaluate the nature of cancer.

Analyzing tumors from dozens of tissue types, Isaac S. Kohane of the Harvard-MIT Division of Health Sciences and Technology has catalogued surprising yet familiar patterns of gene activity in cancer cells—they are the same programmed genetic instructions active during various stages of embryonic and fetal development. Entire suites of genes that drive an embryo's early growth and the later formation of limbs and other structures in the womb normally go silent during the rest of life, but these genetic programs are switched back on in many tumor cells.



LIKE A CANCER: **Genetic programs governing this early embryo may also promote the growth of tumors.**

YORGOS NIKAS *Photo Researchers, Inc.*

Grouping tumors according to the developmental stage their gene activity most resembles reveals predictive information about those tumors, Kohane has found. In groups of lung tumors, for instance, "malignancy and even time to death of actual patients were directly proportional to the 'earliness' of the gene signatures," he says.

In his largest and latest tumor study, Kohane showed that the same holds true across different types of cancer. Comparing gene activity for nearly three dozen kinds of cancer and precancerous conditions against a timeline of 10 developmental processes, he could group seemingly disparate diseases into three categories. Among the tumors with signatures characteristic of the earliest embryonic development stages were lung adenocarcinoma, colorectal adenoma, T cell lymphomas and certain thyroid cancers. The highly aggressive cancers in this group also tend to look most undifferentiated and embryonic. The tumors with gene signatures that mirrored third-trimester and neonatal developmental gene expression patterns tend to be slower-growing types, including prostate and ovarian cancers, adrenal adenoma and liver dysplasia. A third category of tumors represented a mixed bag, in which activity matched aspects of both the other two groups.

Similarities between embryos and tumors "should be paid attention to," says pioneering cancer researcher Lloyd J. Old, chairman of the Ludwig Institute for Cancer Research New York Branch. "The reason this is so interesting is that the idea that cancer and development are in some way linked goes way back," he explains. The 19th-century pathologist John Beard, for example, noted the similarity between tumors and the trophoblast, a part of an early embryo that eventually becomes the placenta. "If you've ever seen the trophoblast invading the uterus, it invades, spreads, creates a blood supply. It also suppresses the maternal immune system," Old says. "All of those are characteristics of cancer."

In his own research, Old has found common genetic programs at work in tumor cells and gametes. One subject of his immunology studies are the cancer/testis (CT) antigens, a group of proteins manufactured almost exclusively by tumors and by sperm- and egg-producing germ-line cells. The specificity of CT antigens makes them ideal targets for cancer vaccines or antibody-based drugs, Old says; moreover, the activation of CT genes in tumors is telling. "These are programs that you and I used as gametes," he explains. Seeing these primordial programs reactivated in tumors has led Old to describe cancer as a "somatic cell pregnancy."

The fact that cancer cells switch on these normally silenced programs suggests to Old that the important characteristics of cancers are not random. "This is a fundamentally different way of thinking. A cell that mutates looks for genes that can help it flourish" and finds them in the suites of developmental genes, he says. "It's a programmatic origin rather than a Darwinian origin" for cancer traits.

The two views of malignancy, however, do not necessarily conflict. "It's not as if accumulating mutations are at odds with the discernible program," remarks Robert A. Weinberg of the Massachusetts Institute of Technology, noting that the activation of developmental programs could be a downstream consequence of the mutations. Weinberg showed last year that gene activity involved in maintaining embryonic stem cell identity is a common feature of the most undifferentiated-looking and aggressive tumors. Whether that kind of evidence indicates an embryonic program driving those cancers remains to be determined, he cautions: "It's an interesting concept, but at this stage what they talk about is highly speculative. One can ascribe all manner of human traits to cancers and speculate that it will lead one into therapeutic insights. But the devil is in the details."

## Arresting Cancer's Development

Evidence is growing that tumor cells may grow and spread by co-opting the genetic programs normally active only during embryonic and fetal development. If true, then disrupting those programs with gene-silencing therapy could undermine a tumor's most threatening traits. Isaac S. Kohane of the Harvard-MIT Division of Health Sciences and Technology has organized cancers into three groups that correlate with different embryonic stages. He suggests that at the very least, drugs already known to work well on one cancer in his groupings should be tested against other cancers with the same profile. *—C.S.*

MICROBIOLOGY

# Don't Talk, Reproduce

**Quiet bacteria devoted to growth could beat antibiotic resistance**

BY MELINDA WENNER

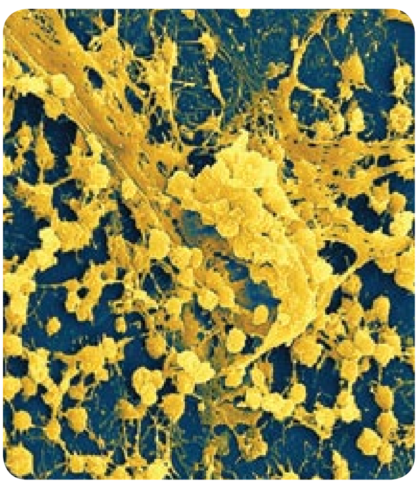
Despite the rising menace of bacteria—at roughly 19,000 a year, more Americans die from drug-resistant *Staphylococcus aureus* infections than from HIV/AIDS—the microorganisms do deserve some credit for their cleverness. Antibiotic-resistant strains reared their heads 60 years ago, and ever since scientists have been struggling to develop second-generation drugs that attack not the bacteria themselves—which promotes resistance—but rather their cell-to-cell communication with one another. Progress has been slow, however, as bacteria have once again proved more complex than anticipated. But now insights from social evolutionary biology may finally point the way to outsmarting the microbes—by exploiting certain members to undermine the entire group.

Forty years ago scientists discovered that some bacteria send and receive messages—in the form of small molecules—to and from surrounding cells. This kind of communication, called quorum sensing, enables bacteria to monitor their population density and to modulate their behavior accordingly. When there are enough cells around to create a "quorum," bacteria begin producing proteins known as virulence factors that sicken their hosts. They can also grow into aggregates called biofilms that render them up to 1,000 times more resistant to antibiotics.

Quorum sensing is now known to be widespread in the bacterial world, and many researchers hope to develop ways to disrupt it. Kim Janda, a chemical biologist at the Scripps Research Institute in La Jolla, Calif., calls this strategy a "stealth approach." Antibiotics kill bacteria or prevent them from growing, enabling resistant mutants to thrive; drugs that disrupt quorum sensing, on the other hand, would spare the microbes' lives, simply preventing them from causing disease or building biofilms.

The problem is that good quorum-sensing inhibitors have been hard to find. The molecules that bacteria use for communication are often species-specific, so developing universal inhibitors is difficult. Moreover, disruptors found to work well in animals have proved toxic to humans. And some researchers worry that these drugs would be efficacious only at the start of an infection, before a quorum had been reached. As a result of these challenges, few pharmaceutical companies have invested in communication-related drug strategies. "People are a little wary of it," says Helen Blackwell, a chemist at the University of Wisconsin–Madison.

In January, however, University of Edinburgh evolutionary biologist Stuart West and his colleagues announced that they had devised a new idea based on a known quorum-sensing nuance: not all bacteria in a given population communicate normally. So-called signal-blind mu-



**BIOFILM** of ***Staphylococcus*** **forms when the bacterial population reaches a "quorum."**

PHOTO RESEARCHERS, INC.

tants produce low-level signals but do not respond to them, whereas signal-negative mutants respond to signals but do not produce them.

These cheats still reap the benefits of quorum sensing because their neighbors cooperate, but they conserve a lot of energy relative to their peers. As a result, they thrive and replicate quickly—causing subsequent generations to contain larger and larger proportions of cheats. But once these cheats become too prevalent, communication is so rare that the population cannot reach a quorum, and its overall virulence drops.

West and his colleagues recently infected a group of mice with normal *Pseudomonas aeruginosa*—a bacterium commonly associated with hospital infections—and infected two other groups with mixtures of half normal *Pseudomonas* and half signal-blind or signal-negative cheats. Seven days later the mice infected with the mixtures were twice as likely to be alive as compared with the mice infected with normal strains. "It seems crazy, but it's feasible to think that maybe if you've got an infection, you could put in a mutant social cheat," and it could help cure you, West says.

Such a therapeutic will not be available anytime soon though, West admits. For one thing, it could be difficult for people—let alone regulatory agencies—to accept the idea of treating infections with more bacteria. Still, he and his colleagues have applied for a patent on the concept, and they are also pursuing a related "Trojan horse" idea in which they try to use mutants to introduce specific genes into a population. "Suppose you have an infection, and it's antibiotic-resistant," West explains. "You get a cheat that is susceptible to antibiotics and then let that spread," and soon the population could be treatable with existing drugs.

Even if these particular strategies do not pan out, researchers in the field are confident that more traditional quorum-sensing inhibitors will. Janda, for one, is developing bacterial "vaccines" that help the immune system recognize and eliminate the molecules produced during quorum sensing. He and others—including Princeton University biologist Bonnie Bassler—are also working with a molecule called AI-2 that they believe is used by many types of bacteria as a signaling molecule and thus could be a universal inhibitor. And Blackwell has found hundreds of small molecules that closely but not completely mimic various signaling chemicals; introduced into a population, such molecules could break down communication. "The promise is huge," she says. "We're going forward unabashed."

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

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## AGING

# Free Radical Shift

**Antioxidants may not increase life span** BY KATE WILCOX

Companies have started putting antioxidants in goods as different as face creams and soda, claiming that they clean out cells, prevent cancer and even stave off death. The idea is to prevent unstable oxygen molecules, which are normal by-products of metabolism, from damaging cells. But a recent study suggests that when it comes to living longer, those antioxidants may not be the answer.

The antioxidant theory of aging states that some of the oxygen molecules used by the body become negatively charged, making them reactive. As a result, they compromise health and age the body by damaging cell structures, proteins and DNA. Cells have a natural defense—superoxide dismutase (SOD), a special class of antioxidant that neutralizes the chemicals and prevents them from harming cells. According to the theory, proposed in 1956 by Denham Harman, now emeritus professor of medicine at the University of Nebraska, when the body gets older, SODs become less efficient at preventing oxidative stress. Over the past 50 years this widely accepted theory has held up in studies: when the SOD gene is knocked out in mice, flies or yeast, the organisms develop cancers and have shorter life spans.

**ANTIOXIDANTS, abundant in pomegranates, counter free radical damage but may not delay aging.**

CORBIS

But in the February *PLoS Genetics,* Siegfried Hekimi and Jeremy M. Van Raamsdonk, both at McGill University, report that removing SODs from tiny *Caenorhabditis elegans* soil worms has the exact opposite effect—they live longer. In the experiment, each of the worms' five SOD genes, which primarily work in the mitochondria (the cells' energy-producing organelles), was disabled in different combinations, hampering the worms' ability to make the antioxidant. When the researchers turned off one SOD gene (namely, *sod-2*), the nematodes actually lived 30 percent longer. When four were disabled in follow-up work, the worms still had a normal life span.

Hekimi believes that the findings

throw a wrench in the entire free radical theory of aging. Instead he claims that cell damage is a product of aging, not the actual cause. "It's like the sun coming up every morning—they can't prove that it will," he says in reference to free radical proponents. "But I have to prove that it won't."

These modified worms are not healthy, though; they show evidence of oxidative stress. Without the antioxidants, their cells are left unprotected, and outside the lab the worms would have died from disease or cancer. But Hekimi separates such a condition from having a normal life span. The organism may be sicker, he observes, but it is living longer.

Other scientists doubt that the findings discredit free radicals entirely. "You can't take a single paper studying a single gene in a single organism and make sweeping conclusions about a theory," remarks John Phillips of the University of Guelph in Ontario, who has examined SODs in the fruit fly *Drosophila melanogaster*. Moreover, *C. elegans* has five SOD genes, whereas humans have two. "I think we need to know where the extra SODs are operating, like in tissues or muscles, and in which cellular compartments" to fully understand oxygen metabolism in *C. elegans*, Phillips says. Knowing the biological idiosyncrasies in the worm would elucidate how SODs work in general.

Hekimi proposes that his findings could bolster an alternative aging theory—specifically, the idea that a slower metabolism or lower temperatures decelerate the body and allow an organism to live longer. Several studies have challenged the rate of living theory of aging, but Hekimi thinks that "you have to take a broader version of the theory, that the rate at which things happen affects life span." As he sees it, in SOD-deficient worms, free radicals damage the mitochondria, which produce less energy and thereby slow the organism down.

Hekimi's idea stands in contrast with that of Bart Braeckman of Ghent University in Belgium, whose own 2007 experiments with *C. elegans* led him to rule out the metabolic theory of aging. But Braeckman also does not think that the free radical theory is the only answer. He notes that Hekimi's work joins other recent studies that challenge the simplistic version of the theory. "The final conclusion was similar in all these papers: there is a problem with the free radical theory," he states.

So what does this mean for the antioxidants everyone clamors for? Synthetic antioxidants have failed to show any clear longevity benefit to humans, and that has been a problem for Harman ever since he conceived his theory. Although antioxidants definitely prevent damage, there is still no consensus on how much they forestall aging. "I'm glad there are challenges to the theory," Harman says. "It's the only way we get anything done."

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NEUROBIOLOGY

# Turn It Up, Dear

**Could growing clinical use of brain electrodes lead to a sex chip?** BY GARY STIX

A fundamental goal of neuroscience has always been to deduce the brain systems that underlie such basic drives as hunger, thirst and sex. In 1956 the well-known physiologist James Olds wrote an article for *Scientific American*, called "Pleasure Centers in the Brain," that described how a rat kept without food for a day was lured down a platform by a tasty meal. En route to dinner, it received a pleasurable electric shock. The rat never showed up for mealtime, instead choosing to delight in the arousal. With the optimism characteristic of that era, Olds concluded that stimulation experiments would lead to an understanding of neural functioning that would allow "one drug that will raise or lower thresholds in the hunger system, another for the sex-drive system, and so forth."

Fifty years later the promise of Olds's vision has yet to fully materialize. Better drugs are needed to suppress appetite and spark sexual desire. But fascination has grown in recent years with taking Olds's more direct route of stimulating the central nervous system.

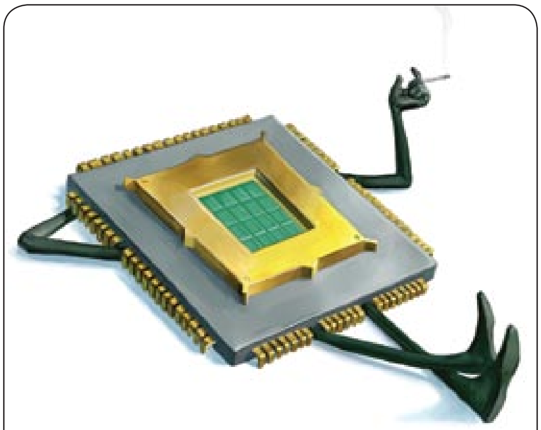
So far no one has created anything like the Orgasmatron, first seen in Woody Allen's 1973 comedy *Sleeper*. Undaunted, one clinician—who has trademarked the name Orgasmatron—ran a small, FDA-reviewed pilot trial to test the possibility of applying electric current to the spine to reverse sexual dysfunction. Stuart Meloy, a North Carolina physician who specializes in implanting spinal electrodes to alleviate pain, found by chance that a slightly off-kilter placement in the lower spine caused one woman to exclaim: "You're going to have to teach my husband to do that."

In 2006 Meloy reported that 10 of 11 women who stopped having or never had orgasms experienced sexual arousal with the temporary implant and, of that group, four had their ability to experience orgasm restored. Meloy is seeking a medical device manufacturer to bring the costs down to $12,000 for a permanent implant, about the charge for breast enlargement.

Neural electrodes may eventually move up the spinal cord to what is often characterized as the body's primary erogenous zone. Deep-brain stimulation, the placing of electrodes at strategic spots far underneath the skull, now treats a variety of ailments, including Parkinson's disease and dystonia (uncontrollable twisting of a body part caused by involuntary muscle contractions). An occasional side effect is spontaneous sexual stimulation.

Tipu Aziz, a neurosurgeon at the University of Oxford, speculates that better knowledge of the brain's pleasure centers—combined with improved surgical procedures and control of electrical pulses—may make a sex chip in the brain a reality. "Lack of sexual pleasure is a huge loss in one's life, and if one could restore that, that would enhance someone's quality of life enormously," Aziz remarks.

Some neuroscientists are not so sure. Morten L. Kringelbach, a researcher at Oxford who sometimes collaborates with Aziz and wrote the book *The Pleasure Center* (Oxford University Press, 2008), cautions that hedonic experience may consist of an impulse corresponding to "wanting" and another that represents "liking." To succeed as a therapy, a sex chip would have to address the challenge of switching on neural circuits that activate both impulses. In a 2008 paper in *Psychopharmacology* with University of Michigan at Ann Arbor psychologist Kent Berridge, Kringelbach illustrated the distinction between the two by citing an infamous case from the 1960s, in which psychiatrist Robert Heath placed "pleasure electrodes" in the brain of a gay man code-named B-19, in part, as an attempt to "cure" his homosexuality.



SEX CIRCUIT: **A pleasure center in the brain may be stimulated by signals from a chip that are then sent to electrodes that zap just the right spot.**

MATT COLLINS

The patient pressed a button compulsively to turn on an electrode that induced a desire for sex, but whether he actually enjoyed the sensation was unclear. The stimulation alone did not induce orgasm, and B-19 never expressed any real contentment while hitting the button. Kringelbach warns against similar misuses of contemporary deep-brain stimulation. "It's important that we not get carried away by this technology," he says. "It's important that we not end up in another era of psychosurgeries," referring to the mid-20th century popularity of lobotomies to treat psychiatric disorders.

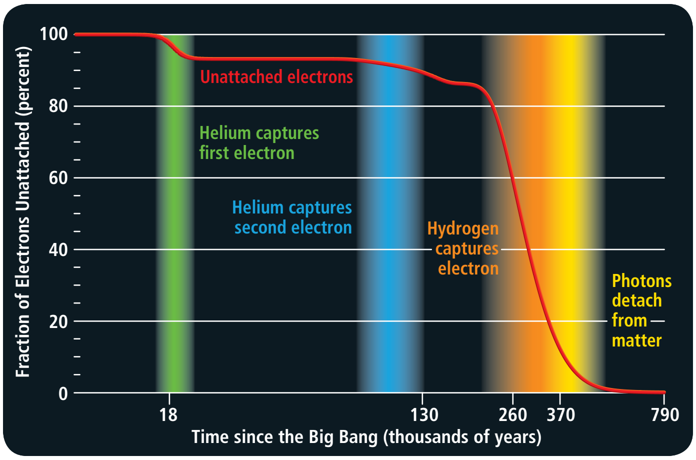
In the end, a sex chip may serve as a prop for moviemakers, but turning on the current may never become a truly practical means of adding the buzz back in your love life.

COSMOLOGY

# Spectral Sensation

**New way to squeeze information from the microwave background** BY GEORGE MUSSER

Cosmologists talk about the cosmic microwave background radiation, their snapshot of the universe at the tender age of 400,000 years, so much that it might seem pretty well mined out by now. After all, the European Space Agency intends for its new Planck satellite to extract "essentially all the information available" in the radiation's spatial patterns. But cosmologists looking beyond Planck say the radiation has a barely explored aspect that, if it could be observed with enough precision, would reveal new details about the early universe: its spectrum.




ATOMS formed in stages as the universe cooled enough for nuclei to snap up electrons. In the process they emitted photons that future observatories can look for, revealing aspects of the cosmos that now go unseen.

Astronomers routinely use the rainbow of colors emitted by the sun and other stars to determine their composition. At the American Astronomical Society meeting this past January, renowned astrophysicist Rashid Sunyaev of the Max Planck Institute for Astrophysics in Garching, Germany, argued that a successor to Planck might pick up similar fingerprints in the background radiation, the spectrum of which currently seems completely featureless and generic.

In the conventional picture, the background radiation consists of photons produced in the earliest moments of the big bang. They scattered off protons and electrons in a game of cosmological pachinko until everything cooled enough for protons to latch onto electrons and form hydrogen atoms—a process known as recombination. Being electrically neutral, the atoms were less prone to scatter photons. So the photons began to stream across space in more or less straight lines. The pachinko had thoroughly mashed their spectrum, and the only thing cosmologists can glean from it is the overall density of matter.

Yet this picture glosses over two nuances. First, it took a while for protons to get a firm hold on electrons. Their grip was tentative at first. To tighten up, a newly formed atom had to lose energy by emitting photons, and it did so in its own good time. Further complicating matters, a photon from one atom tended to knock the electron off another. Like crabs in a bucket, atoms thwarted one another. What overcame their mutual antagonism was cosmic expansion, which sapped the photons' energy and gradually tilted the balance in favor of atom formation over destruction. The commonly cited time frame of 400,000 years is just a convenient milestone; recombination actually took as long as a couple of million years to run to completion.

The second nuance is that although the universe consisted mostly of hydrogen, it also had a fair amount of helium. With twice the electric charge of protons, helium nuclei had more latching power and formed atoms earlier, catching their first electron at about 15,000 years and their second at 100,000 years. What is more, they avoided the crab bucket syndrome. A small advance guard of hydrogen atoms acted as a moderator, intercepting the photon emitted by one helium atom before it could destroy another. So helium atoms formed snappily.

The photons emitted by hydrogen and helium added some compositional fingerprints to the primordial soup. Measuring the number of photons emitted by helium would nail exactly how much helium the

## Blurring the Cosmic Snapshot

Investigators studying the cosmic microwave background radiation once ignored the nuances of hydrogen and helium formation, because observations were too crude to detect their effects. Improved instruments, however, are forcing theorists to play catch-up. One problem they have found is that the background radiation is actually somewhat blurry. As hydrogen recombination dragged out, photons continued to scatter off charged particles and lost the imprint of fine-scale matter clumps. If cosmologists did not take that process into account, they would mistakenly conclude that the early universe lacked such clumps and adjust their models to eliminate the clumps, skewing estimates of basic parameters such as density. "If you build a very sensitive experiment and have a theoretical model that's erroneous, it would be a sad thing," says cosmologist Eric Switzer of the University of Chicago.

—*G.M.*

SCIENTIFIC AMERICAN; SOURCE: JENS CHLUBA *Canadian Institute for Theoretical Astrophysics,* RASHID SUNYAEV *Max Planck Institute for Astrophysics* AND JOSÉ ALBERTO RUBIÑO-MARTÍN *Institute of Astrophysics of the Canary Islands* universe synthesized—a quantity that now must be extrapolated, with difficulty, from the amount of helium in stars. "This is an absolutely clear way to find the primordial abundance of helium," Sunyaev says. In addition, photons from helium date to an age before the release of the microwave background. They might bear the stamp of processes now hidden from us, such as exotic particle decays.

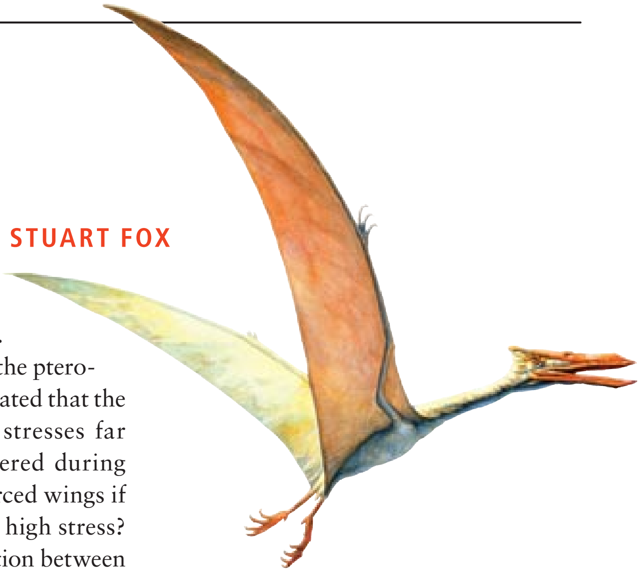
The trouble is that the helium photons are outnumbered a billion to one by primordial photons. Fortunately, because helium atoms formed so rapidly, the photons they emitted are sharply concentrated at certain frequencies, known as spectral lines. Sunyaev and Jens Chluba of the Canadian Institute for Theoretical Astrophysics have urged a new mission to sweep across frequencies looking for a spike in the number of photons, like drawing your finger across a surface to feel a bump too small to measure with a ruler. "To observe these lines, you have to observe a fixed position and scan across frequency," says José Alberto Rubiño-Martín of the Institute of Astrophysics of the Canary Islands. In contrast, existing missions, including the Planck satellite, observe a fixed frequency and scan across position.

In a way, cosmological history is repeating itself. For decades, spatial measurements of the microwave background looked completely uniform until cosmologists spotted the spatial fluctuations. Now spectral measurements look completely uniform. Once cosmologists see spectral fluctuations, they expect another flood of information about the early universe.

PALEONTOLOGY

# Leapin' Lizards

**Biomechanics suggests how a giraffe-size pterosaur took flight** BY STUART FOX



UP, UP AND AWAY: ***Quetzalcoatlus*** **could have gotten airborne by jumping from all fours.**

For almost a century, scientists struggled to explain how the extinct reptiles called pterosaurs managed to get off the ground. In regard to the smaller pterosaurs, bird models sufficed; flapping from standstill or a running start could work. But for the larger pterosaurs, some of which had a 26-foot wingspan and weighed 200 pounds, scientists could not find a bird model that explained takeoff.

That is because they did not take off like birds, thinks Michael Habib, who studies functional anatomy and evolution at Johns Hopkins University. After analyzing the biomechanics of the creatures, Habib proposes that pterosaurs took flight by using all four limbs to make a standing jump into the sky, not by running on their two hind limbs or jumping off a height, as more widely assumed.

"I started as a bird researcher," Habib says. "I became interested in mechanical limits in flying animals, and that naturally leads to pterosaurs."

And pterosaurs such as *Quetzalcoatlus* sit firmly on the far end of those limits. Even with its birdlike hollow bones, *Quetzalcoatlus* weighed between 250 and 550 pounds and had about a 36-foot wingspan. By comparison, an albatross weighs about 18 pounds and has an 11-foot wingspan. It had to take off somehow, but no one had a good guess how.

By analyzing the shape of the pterosaur arm bones, Habib calculated that the forelimbs could withstand stresses far greater than those encountered during flight. But why evolve reinforced wings if they would never experience high stress? Habib then made the connection between the quadrupedal gait of the large pterosaurs and the jumping quadrupedal takeoff he had seen in vampire bats. If the large pterosaurs used all four limbs to get off the ground, that would explain both the superstrong forelimbs and solve the mystery of pterosaur takeoff.

But just because an animal could do something does not mean it did, and some paleontologists remain unconvinced that Habib's data actually explain how pterosaurs got off the ground. "When I read the manuscript, my first reaction was, 'Hmm, that's odd.' But if you work on pterosaurs, you get used to odd things anyway," remarks David Unwin, a paleontologist at the University of Leicester in England and author of the book *The Pterosaurs: From Deep Time.* "Large and giant pterosaurs pose a problem," he explains, "because the flying speed they need to achieve is quite high, 30 or 40 miles per hour, and I have a hard time understanding how they get that fast from a standing jump."

Paleontologist Kevin Padian of the University of California, Berkeley, also questions some of Habib's conclusions. Padian says he believes the smaller pterosaurs (some were the size of sparrows) were bipedal and thus took off with two legs, not four. He also does not think Habib has covered every kind of relevant bone stress.

The divide between the pterosaur researcher and the researcher looking at pterosaurs is fairly common in this area of paleontology. According to both Unwin and Habib, pterosaurs, with their improbable size and ability to fly, draw in biomechanics experts more focused on physics than prehistoric biology. "Because of the bizarre nature of pterosaurs, they've at-

JOE TUCCIARONE *Photo Researchers, Inc.*

tracted attention from outside paleontology," Unwin says. "So we've had a disproportionate number of people come in from outside paleontology, lots of people ready to have a go at the aerodynamics who are not pterosaur researchers first."

Still, all agree that Habib brings up interesting points, and they are not just for biomechanics. Showing that the large pterosaurs could take off without having to jump off a cliff expands the range of places they could have lived, raising all kinds of questions about the ecology of large pterosaurs. Says Padian: "Every time we think we've figured them out, they throw us another curve."

*Stuart Fox, a freelance writer based in New York City, studied pterosaur biomechanics while working at the Field Museum of Natural History in Chicago.*

PHYSICS

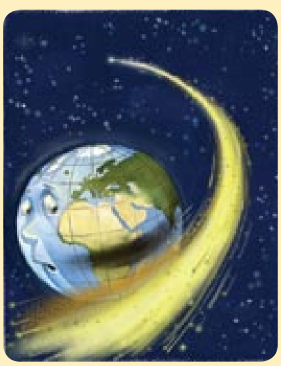
## Logic That Feels the Noise

As microchips shrink, the inescapable electronic buzz that emerges from thermal fluctuations, cross talk between wires and other sources can endanger their proper function. A way around that problem could be stochastic resonance, a phenomenon in which noise can boost a weak signal and improve a system's performance. Certain kinds of structures, such as a sensory nerve, will output a signal only when background noise is sufficiently high. Researchers at Arizona State University constructed logic gates—circuit elements that perform logic functions—that behave in a similar way. When noise levels are low, the gates perform unreliably; however, at the kinds of noise levels expected for the smallest transistors, they work correctly. Such unusual, nonlinear behavior could help microchips get smaller. Moreover, altering certain applied voltages in the circuit can reconfigure the gate on the fly, thereby creating a morphing processor. Tune in to the March 13 issue of *Physical Review Letters* for more details. —*Charles Q. Choi*

### Data Points

## Buzzed

Earth got a close shave from an asteroid similar in size to the one that produced the 1908 Tunguska explosion in Siberia. The object, dubbed 2009 DD45, zipped past on March 2 at about twice the distance of geostationary orbit and only days after its discovery. Its orbit intersects Earth's, but the rock will not get anywhere near this close for another 58 years.



**Approximate diameter of 2009 DD45:** 35 meters

**Speed relative to Earth:** 8.82 kilometers per second

**Closest approach:** 72,200 km

**Geosynchronous orbit:** 35,786 km

**Next near miss:** March 2067

**Closest approach at that time:** 110,682 km

**Explosive force that produced the Tunguska damage:** 10 to 15 megatons

**Number of near-Earth asteroids detected as of March 15, 2009:** 6,043

*SOURCES: NASA Near Earth Object Program; "The Tunguska Mystery," by Luca Gasperini et al., in* Scientific American*; June 2008*

MATT COLLINS

BIOLOGY

## Bug Off

The capability to seek out medicinal plants was thought to be limited to creatures with advanced brains; for instance, chimpanzees harboring intestinal worms swallow bristly leaves to scrape the parasites from their guts. Now researchers at Wesleyan University and their colleagues find that woolly bear caterpillars (*Grammia incorrupta*) also self-medicate when ill. Caterpillars infested with parasitic fly maggots ate roughly twice as much alkaloid (specifically, pyrrolizidine alkaloid) as uninfested ones; such toxins naturally exist in bloodroot and other caterpillar food plants. As a result, roughly 20 percent more of the infested caterpillars survived into adulthood as compared with infested caterpillars that did not munch on the medicine. The findings, the first known instance of invertebrate self-medication, appear in the March 10 *PLoS ONE*. —*Charles Q. Choi*

BEHAVIOR

## Planning of the Apes

A rock-throwing chimp at Sweden's Furuvik Zoo proves that nonhuman primates can plan for the future. For the past several years, Santino has put on a show of dominance every day at around 11 A.M. by yelling and running around, which is typical of male chimps. But he would occasionally lob rocks at zoo visitors. (Fortunately, his aim is terrible, and no one has been seriously hurt.) Workers found that earlier in the morning he would calmly fish his ammunition out of the moat around his habitat and chip away at concrete rocks on his island to form dessert-plate-size disks. Santino would then pile up his weapons. This observation, described in the March 10 *Current Biology*, confirms lab experiments showing that our fellow apes can prepare for upcoming events.

—*Coco Ballantyne*

COURTESY OF FURUVIK ZOO

**AND MY NEXT TARGET IS...: At least it's only rocks that Santino likes to fling at zoo visitors.**

## In Brief

### WHO WOULDN'T LOVE A PONY?

Horse domestication changed the course of human history, and the starting point seems to be at least 5,500 years ago with the Botai people, who lived in what is now northern Kazakhstan. Scientists found evidence of mare milk in nine ancient cooking vessels from the area, as well as damage in 15 horse jaws from bits or bridles, suggesting that the Botai had horse farms. Their findings appear in the March 5 *Science.* —*David Biello*

**MARE MILKING shows up in ancient pottery and suggests domestication.**

### T CELL BOOSTER

Cocktails of antiviral drugs can suppress the AIDS virus and provide a boost to the immune system's T cells, which are depleted by HIV. In some patients who take the cocktail, however, the T cell count remains low, making them vulnerable to opportunistic infections. In a small, early-stage clinical trial, French researchers found that interleukin-7, a growth factor, increased the number of active T cells, suggesting that intermittent shots of the compound could keep an HIV-infected immune system working. The findings appear in the March 16 *Journal of Clinical Investigation.* —*Philip Yam*

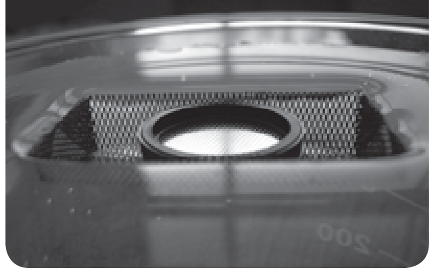
### SUPERNOVAE IN ICE

Ice cores not only contain evidence of past atmospheric conditions, but they also may hold clues about astronomical events. In an Antarctic ice core, researchers in Japan discovered spikes in the concentration of nitrate ions. The spikes coincide with two stellar explosions in the 11th century: one in 1006 and the other in 1054, which created the Crab nebula. Gamma rays from these supernovae could have boosted atmospheric levels of nitrogen oxides that got trapped as nitrate ions in air bubbles in the ice cores. —*John Matson*

MATERIALS

# Float Your Boat

**SUPERBUOYANT MESH holds up a weighty reflective disk.**



Imagine a mesh that instead of letting water in repelled it so much that a life preserver made from it would support a horse. Scientists at the Harbin Institute of Technology in China created such a mesh out of copper wires 200 microns thick and pores about that size or smaller. They dunked the lattice first in silver nitrate solution and then in acid, which deposited the silver onto the copper as leaflike structures seven microns high. Like the hairs on the underside of the great diving beetle *Dytiscus marginalis*, the silver leaves trap a film of air, thereby making the meshes superwater-repellent.

Postage-stamp-size boats made of these lattices could hold three times as much sand as ones made from untreated meshes, and they still floated even when their upper edges dipped below the water's surface. Although the scientists admit that applying their superbuoyant technology to full-size ships would be unlikely—the hydrophobic repulsion is probably too weak for large vessels—they note it could lead to a new generation of miniature aquatic robots. Their work surfaces in the February 25 *Applied Materials & Interfaces*.

—*Charles Q. Choi*

PSYCHOLOGY

# Half Empty or Half Full

People are typically biased toward noticing either good or bad events, and a common genetic variation may underlie such tendencies for optimism or pessimism. Scientists at the University of Essex in England investigated serotonin, a neurotransmitter linked with mood, and explored how 97 volunteers preferred different kinds of images. People who carried only long versions of the gene for the serotonin transporter protein—which controls levels of the neurotransmitter in brain cells—tended to pay attention to pleasant pictures (such as images of chocolate) while avoiding negative ones (such as photographs of spiders). Those with a shorter form showed opposite preferences, though not as strongly. The findings, in the February 25 *Proceedings of the Royal Society B*, help to explain why people may be less prone to anxiety and depression and could lead to therapies that help some look on the bright side. —*Charles Q. Choi*

**WHAT DO YOU PREFER TO LOOK AT? Optimists tend to pay attention to images of chocolate and avoid pictures of spiders; pessimists do the opposite.**

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ALAN K. OUTRAM *AP Photo* (*horse*); COURTESY OF AMERICAN CHEMICAL SOCIETY (*superbuoyant mesh*); DAVID LIITTSCHWAGER *Getty Images* (*spider*); GARETH MORGANS *Getty Images* (*chocolate*)

SciAm Perspectives

# Designing Rules for Designer Babies

**More oversight is needed to prevent misuse of new reproductive technologies**

BY THE EDITORS

On March 3 the cover story of the *New York Daily News* trumpeted a simple imperative to "Design Your Baby." The screaming headline related to a service that would try to allow parents to choose their baby's hair, eye and skin color. A day later the Fertility Institutes reconsidered. The organization made an "internal, self regulatory decision" to scrap the project because of "public perception" and the "apparent negative societal impacts involved," it noted in a statement.

The change of heart will do nothing to stymie the dawning era of what the article called "Build-A-Bear" babies. The use (and abuse) of advanced fertility technology that evokes fears of Gattaca, Brave New World and, of course, the Nazis' quest for a blonde, blue-eyed race of Aryans continues apace. A recent survey found that about 10 percent of a group who went for genetic counseling in New York City expressed interest in screening for tall stature and that some 13 percent said they would be willing to test for superior intelligence. The Fertility Institutes is still building the foundation for a nascent dial-a-trait catalogue: it routinely accepts clients who wish to select the sex of their child.

The decision to scrap the designer baby service came just a few weeks after Nadya Suleman, a single, unemployed California mother living on food stamps, gained notoriety after giving birth to octuplets through in vitro fertilization. The Suleman brouhaha showed that even routine uses of reproductive technologies can be fraught with issues that bear on ethics and patient safety.

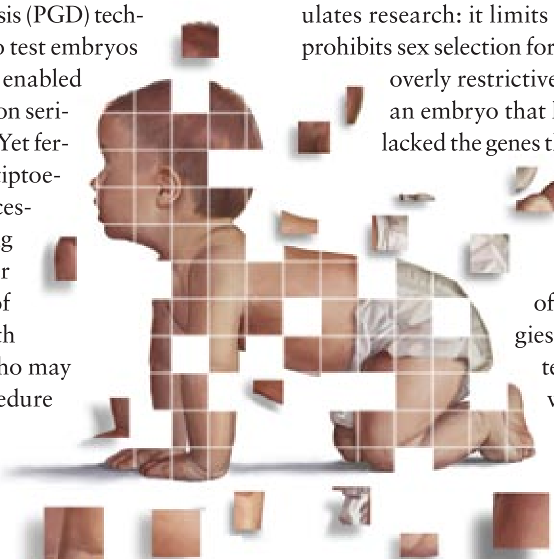
The preimplantation genetic diagnosis (PGD) technique used by the Fertility Institutes to test embryos before implantation in the womb has enabled thousands of parents to avoid passing on serious genetic diseases to their offspring. Yet fertility specialists are doing more than tiptoeing into a new era in which medical necessity is not the only impetus for seeking help. In the U.S., no binding rules deter a private clinic from offering a menu of traits or from implanting a woman with a collection of embryos. Physicians who may receive more than $10,000 for a procedure serve as the sole arbiters of a series of thorny ethical, safety and social welfare questions. The 33-year-old Suleman already had six children, and her physician implanted her with six embryos, two of which split into twins. American Society for Reproductive Medicine (ASRM) voluntary guidelines suggest that, under normal circumstances, no more than two embryos be transferred to a woman younger than 35 because of the risk of complications.

Of course, any office consultation with a fertility doctor will likely neglect the nuances of more encompassing ethical dilemmas. Should parents be allowed to pick embryos for specific tissue types so that their new baby can serve as a donor for an ailing sibling? For that matter, should a deaf parent who embraces his or her condition be permitted to select an embryo apt to produce a child unable to hear? Finally, will selection of traits perceived to be desirable end up diminishing variability within the gene pool, the raw material of natural selection?

In the wake of the octuplets' birth, some legislators made hasty bids to enact regulation at the state level—and one bill was drafted with the help of antiabortion advocates. The intricacies of regulating fertility technology requires more careful consideration that can only come with a measure of federal guidance. As part of the push toward health care reform, the Obama administration should carefully inspect the British model.

Since 1991 the U.K.'s Human Fertilization and Embryology Authority (HFEA) has made rules for in vitro fertilization and any type of embryo manipulation. The HFEA licenses clinics and regulates research: it limits the number of embryos implanted and prohibits sex selection for nonmedical reasons, but it is not always overly restrictive. It did not object to using PGD to pick an embryo that led to the birth of a girl in January who lacked the genes that would have predisposed her to breast cancer later in life.

HFEA may not serve as a precise template for a U.S. regulatory body. But a close look at nearly two decades of licensing a set of reproductive technologies by the country that brought us the first test-tube baby may build a better framework than reliance on the good faith of physicians who confront an inherent conflict of interest. ■


MATT COLLINS

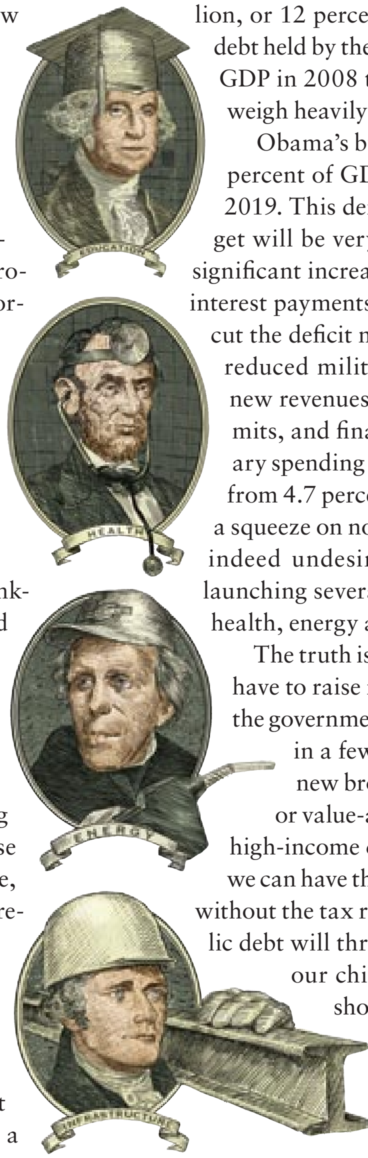
## Sustainable Developments

# Paying for What Government Should Do

**Obama's reexpansion of the government's economic role is vital—and we will have to pay for it**

BY JEFFREY D. SACHS

**The 10-year budget framework that President** Barack Obama released in February, called "A New Era of Responsibility," is as much a philosophy of government as a fiscal action plan. Gone is the Ronald Reagan view that "government is not the solution to our problem; government is the problem." Obama rightly sees an expanded role for government as vital to meeting the 21st-century challenge of sustainable development.



The scientific discipline known as public economics describes why government is needed alongside markets to allocate resources. These reasons include the protection of the poor through a social safety net; the correction of externalities such as greenhouse gas emissions; the provision of "merit goods" such as health care and education that society deems to be essential for all its members; and the financing of scientific and technological research that cannot be efficiently captured by private investors. In all these circumstances, the free-market system tends to underprovide the resource in question.

Reagan came to office in 1981 on a platform of shrinking the public sector to free resources for market-based resource allocation. Federal revenues and outlays remained relatively unchanged as a share of national income from 1981 to 2008, at around 18 percent of gross domestic product (GDP) for revenues and around 21 percent of GDP for outlays. The U.S. ran budget deficits during most of that period, with a long and chronic stalemate between those who would raise taxes and those who would cut spending. By and large, the public resisted cuts to spending programs but also resisted calls for tax increases.

The result is in strong contrast with Europe. Federal, state and local government revenues in the U.S. are about 33 percent of gross domestic product, compared with 45 percent in Europe; spending stands at 39 percent of GDP in the U.S. and 46 percent in Europe. Yet because U.S. taxes are even lower than spending as a share of GDP, U.S. deficits are chronically higher.

Obama's budget plan properly focuses on areas that public economics identifies as priorities: health, education, public infrastructure, and research and development, especially sustainable energy—all areas where the U.S. lags discernibly behind many parts of Europe. The president's vision of an expanded federal role is on target and transformative, but the financing will be tricky. This year's deficit will reach an astounding $1.75 trillion, or 12 percent of GDP. In the plan, the government debt held by the public will balloon from 40.8 percent of GDP in 2008 to 65.8 percent in 2013, a level that will weigh heavily on the budget for years.

Obama's budget plan aims to reduce the deficit to 3 percent of GDP by 2013 and then to level it off until 2019. This deficit is relatively large, but even that target will be very difficult to achieve and sustain. With significant increases in entitlements spending and higher interest payments on the rising public debt, the plan is to cut the deficit mainly through higher taxes on the rich, reduced military outlays for Iraq and Afghanistan, new revenues from auctioning carbon emissions permits, and finally a squeeze on nondefense discretionary spending as a share of GDP (which is set to decline from 4.7 percent in 2010 to 3.3 percent in 2019). Such a squeeze on nondefense spending seems unlikely—and indeed undesirable—at a time when government is launching several much needed programs in education, health, energy and infrastructure.

The truth is that the U.S., like Europe, will probably have to raise new revenues by a few percent of GDP if the government is to carry out its expanded role. Within a few years we will probably see the need for new broad-based taxes: perhaps a national sales or value-added tax such as those common in other high-income countries. If we continue to assume that we can have the expanded government that we need but without the tax revenues to pay for it, the buildup of public debt will threaten the well-being of our children and our children's children. No parent, or citizen, should find such an approach acceptable. ■

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

SCI AM An extended version of this essay is available at **www.SciAm.com/may2009**

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

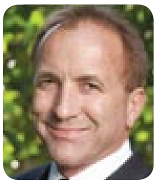
  

## Skeptic

# Creationism in 3-D

**A skeptic engages three types of creationists who claim science supports their beliefs, yet they contradict one another**

BY MICHAEL SHERMER



**During the tsunami of bicentennial celebrations of** Charles Darwin's 200th birthday in February, I visited the fringes of evolutionary skepticism to better understand how one of science's grandest theories could still be doubted.

Noah's Ark Zoo Farm in Bristol, England, is run by a kindly gentleman named Anthony Bush, who insisted that I not confuse him with those "loony American creationists" who think that Earth is only 6,000 years old. "How old do you think it is?" I queried. "Oh, I've worked it out to be around 100,000 years old, with Adam and Eve at around 21,000 years old." (At an order of magnitude difference that makes Mr. Bush only five zeros shy of reality.)

What about, I pressed on, all the geologic evidence for a much older Earth? All those strata of, say, sandstone—loose sand compressed into solid rock over immense periods? Those strata are laid down every season, like tree rings, Bush explained. Interesting analogy, given that we can see trees growing from year to year, but where can we find sand being annually compressed into stone?

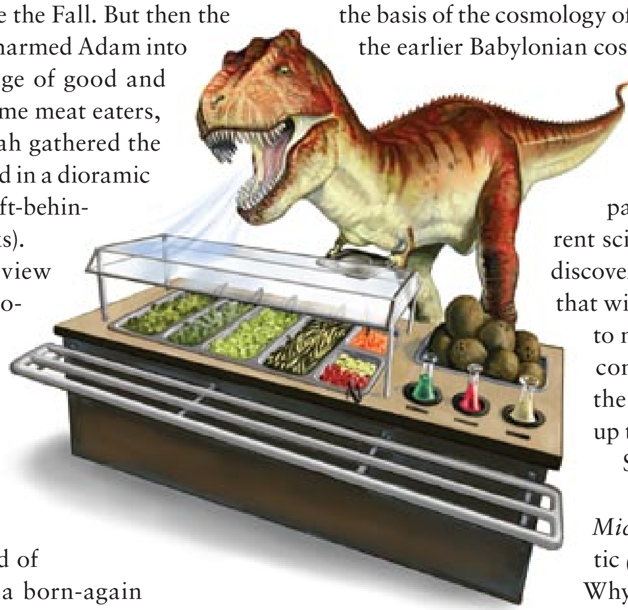
At the Creation Museum in Petersburg, Ky., I learned that Earth was created in 4004 B.C., about the same time that the Mesopotamians invented beer ("That's on the secular timeline," I was told). Dioramas feature children frolicking among vegetarian dinosaurs, including a *Tyrannosaurus rex* and *Utahraptor,* whose daggerlike teeth and claws, it was noted, were used for cracking open coconuts before the Fall. But then the snake tempted Eve, who in turn charmed Adam into tasting the fruit of the knowledge of good and evil—after which dinosaurs became meat eaters, humans became sinners and Noah gathered the animals into the Ark (also rendered in a dioramic drama complete with screaming left-behinders on soon-to-be swamped rocks).

My tour ended with an interview with Georgia Purdom, an accommodating and bright woman (Ph.D. in molecular genetics from Ohio State University) who explained that the worldview you hold (biblical versus secular) determines how you interpret the data.

I countered by pointing out that Francis Collins, former head of the Human Genome Project, is a born-again evangelical Christian who fully accepts evolution. In his book *The Language of God* (Free Press, 2007), Collins describes ancient repetitive elements (AREs) in DNA that arise from "jumping genes" that copy and insert themselves in other locations in the genome, usually without any function. When you align sections of human and mouse genomes, the AREs are in the same location. "Unless one is willing to take the position that God has placed these decapitated AREs in these precise positions to confuse and mislead us," he asserts, "the conclusion of a common ancestor for humans and mice is virtually inescapable."

Collins is wrong, Purdom stated, because "he does not accept the biblical history in Genesis, so he's beginning with his ideas about what happened in the past rather than what God said happened in the past, so he's interpreting that data in light of that starting point."

Shoehorning science into scripture was also painfully on display at the University of North Florida, where I debated founder and chief biblical cosmologist of Reasons to Believe Hugh Ross, an Old Earth Creationist who thinks that the biblical authors describe the expanding universe in such passages as Job 9:8, where God "stretched out the heavens," and Isaiah 40:22, where God "stretcheth out the heavens as a curtain, and spreadeth them out as a tent to dwell in." The key word in Hebrew is *natah,* which means "spread out," like a blanket or a tent, and is a metaphor for the dome or canopy of the sky and fixed stars that formed the basis of the cosmology of the ancient Hebrews, derived from the earlier Babylonian cosmology during the Jewish captivity in Mesopotamia.



In my opinion, Ross employs the hindsight bias when he digs through the scriptures in search of passages that vaguely resemble current scientific findings. Had cosmologists discovered that we live in a closed universe that will eventually collapse, then it seems to me that Job 9:7 would work well by confirming that God "commandeth the sun, and it riseth not; and sealeth up the stars."

Seek and ye shall find. ■

*Michael Shermer is publisher of* Skeptic *(www.skeptic.com) and author of* Why Darwin Matters.

PHOTOGRAPH BY BRAD SWONETZ; ILLUSTRATION BY MATT COLLINS

## Anti Gravity

# The Bradypus Bunch

**A living Muppet among the tropical treetops**

BY STEVE MIRSKY

**Life is going to present special challenges to any** creature named for a deadly sin. Sloths really deserved better. They could have been called deliberates or contemplatives. How sloths conceive of themselves remains a secret—three-toed sloths (*Bradypus variegatus*) seem to smile a lot, but they're not talking.

They didn't say anything to me, anyway, at the Aviarios Sloth Rescue Center just north of Cahuita, along the Caribbean coast of Costa Rica, which I visited on March 6. How I got to Aviarios is a story of hardship and struggle. Not on my part, of course. I'm talking about the incredibly diligent and attentive staff on the luxury cruise ship *Zuiderdam,* which left Fort Lauderdale on February 27 for the Bahamas, Aruba, Curaçao, Panama and Costa Rica before returning to Florida. The biggest test of *my* mettle was seeing whether I could finish yet another extravagant dinner. If the creatures slowly digesting leaves in the trees of the Aviarios sanctuary are sloths, call me glutton. (Which, coincidentally, is the opening line of my planned novella *Mopey Doc,* about a melancholy physician with a body mass index of 37.)

The trip was the third in a continuing series of Scientific American cruises put together by InSight Cruises, in which a sterling faculty of expert scientists and the occasional freeloading journalist lecture to an enthusiastic and well-adapted audience. On this creative and intelligently designed voyage, the theme was evolution.

Along the way, the ship was lifted 85 feet in the legendary Gatun Locks, the Atlantic-side steps of the Panama Canal, into the vast Gatun Lake. Four cruise lecturers then took a small motorboat across the lake's choppy surface to tour Barro Colorado Island, home to the Smithsonian Tropical Research Institute. A century ago, before the flooding of the island's valley as part of the canal's construction, Barro Colorado was a hilltop. Now it's a giant island laboratory (that's also home to sloths). A historic three-decades-old research effort includes tagging and periodically evaluating every single plant—a quarter of a million currently—on part of the island to try to get a picture of how tropical biodiversity is established and maintained. All that foliage provides ample cover for countless ticks, some of which temporarily enjoyed my patronage while masquerading as freckles.

The day after going through the Gatun Locks, I was face to incredibly cute face with Buttercup, the original rescued sloth at the Aviarios center. Husband-and-wife team Luis Arroyo and Judy Avey-Arroyo were bed and breakfast proprietors in 1992 when three neighborhood children brought them Buttercup, then an orphaned infant. The Arroyos nursed the three-fingered sloth to a healthy adulthood and became known as sloth savants. When local people found hurt or orphaned sloths, they brought them to Luis and Judy. By 1997 the Arroyos were in the sloth-saving business full-time.

The challenges are constant, as the scientific literature on sloths is sparse. The Arroyos are attempting basic studies, for example, on the makeup of sloth milk. Babies being fed by their mother "gain weight sometimes three or four times faster than the orphans we're hand-raising," Judy says. "So mother's milk has something—maybe a high fat content. Our milk study has failed so far because we can't take enough milk from the mother to analyze." And that's because mothers don't bother to store milk, as the baby is always right there, hanging on. In business jargon, sloth milk production is a just-in-time inventory strategy—foxes may have the rep, but it's sloths that are sly.

Despite their name, sloths are actually real go-getters, sleeping only about 10 hours a day as compared with the 24, minus meal breaks, of your average house cat. Their Muppety, monkey-like appearance belies their true taxonomical standing, more closely related to anteaters and even armadillos. And a sloth does indeed spend most of its time in the canopy, coming down to ground level about once a week to urinate and defecate. Its lifestyle is thus eerily similar to a rare variety of primate, the New York City penthouse-dwelling supermodel.

Today 116 sloths are either passing through for treatment at the Aviarios Slothpital before returning to the treetops or living out their lives with the Arroyos. Some sloths are orphaned, some are injured coming into contact with electrical lines, and some are attacked by humans attempting to give a sad, second meaning to Charles Darwin's *The Descent of Man*. For information on the Aviarios' rescue center and its highly evolved mission, go to www.slothrescue.org ■

PHOTOGRAPH BY FLYNN LARSEN; ILLUSTRATION BY MATT COLLINS

# The Planetary Air Leak

## As Earth's atmosphere slowly trickles away into space, will our planet come to look like Venus?

## By David C. Catling and Kevin J. Zahnle

### KEY CONCEPTS

- Many of the gases that make up Earth's atmosphere and those of the other planets are slowly leaking into space. Hot gases, especially light ones, evaporate away; chemical reactions and particle collisions eject atoms and molecules; and asteroids and comets occasionally blast out chunks of atmosphere.
- This leakage explains many of the solar system's mysteries. For instance, Mars is red because its water vapor got broken down into hydrogen and oxygen, the hydrogen drifted away, and the surplus oxygen oxidized—in essence, rusted—the rocks. A similar process on Venus let carbon dioxide build up into a thick ocean of air; ironically, Venus's huge atmosphere is the result of the *loss* of gases.

*—The Editors*

One of the most remarkable features of the solar system is the variety of planetary atmospheres. Earth and Venus are of comparable size and mass, yet the surface of Venus bakes at 460 degrees Celsius under an ocean of carbon dioxide that bears down with the weight of a kilometer of water. Callisto and Titan—planet-size moons of Jupiter and Saturn, respectively—are nearly the same size, yet Titan has a nitrogen-rich atmosphere thicker than our own, whereas Callisto is essentially airless. What causes such extremes? If we knew, it would help explain why Earth teems with life while its planetary siblings appear to be dead. Knowing how atmospheres evolve is also essential to determining which planets beyond our solar system might be habitable.

A planet can acquire a gaseous cloak in many ways: it can release vapors from its interior, it can capture volatile materials from comets and asteroids when they strike, and its gravity can pull in gases from interplanetary space. But planetary scientists have begun to appreciate that the escape of gases plays as big a role as the supply. Although Earth's atmosphere may seem as permanent as the rocks, it gradually leaks back into space. The loss rate is currently tiny, only about three kilograms of hydrogen and 50 grams of helium (the two lightest gases) per second, but even that trickle can be significant over geologic time, and the rate was probably once much higher. As Benjamin Franklin wrote, "A small leak can sink a great ship." The atmospheres of terrestrial planets and outer-planet satellites we see today are like the ruins of medieval castles—remnants of riches that have been subject to histories of plunder and decay. The atmospheres of smaller bodies are more like crude forts, poorly defended and extremely vulnerable.

Recognizing the importance of atmospheric escape changes our perspective on the solar system. For decades, scientists have pondered why Mars has such a thin atmosphere, but now we wonder: Why does it have any atmosphere left at all? Is the difference between Titan and Callisto a consequence of Callisto's losing its atmosphere, rather than of Titan having been born of airier stuff? Was Titan's atmosphere once even thicker than it is today? How did Venus steadfastly cling to its nitrogen and carbon dioxide yet thoroughly lose its water? Did escape of hydrogen help to set the stage for complex life on Earth? Will it one day turn our planet into another Venus?

### When the Heat Is On

A spaceship that reaches escape velocity is moving fast enough to break free of a planet's gravity. The same is true of atoms and molecules, although they usually reach escape velocity less purposefully. In thermal escape, gases get too hot to hold on to. In nonthermal processes, chemical or charged-particle reactions hurl out atoms and molecules. And in a third process, asteroid and comet impacts blast away the air.

Thermal escape is, in some ways, the most common and straightforward of the three. All bodies in the solar system are heated by sunlight. They rid themselves of this heat in two ways: by emitting infrared radiation and by shedding matter. In long-lived bodies such as Earth, the former

ALFRED T. KAMAJIAN

LOSS OF CERTAIN GASES, especially hydrogen, has transformed Earth. It is one of the reasons that oxygen built up in the atmosphere. In the future, the depletion of hydrogen will dry out our oceans and all but shut down geologic cycles that stabilize the climate. Life may still be able to hold out in the polar regions.

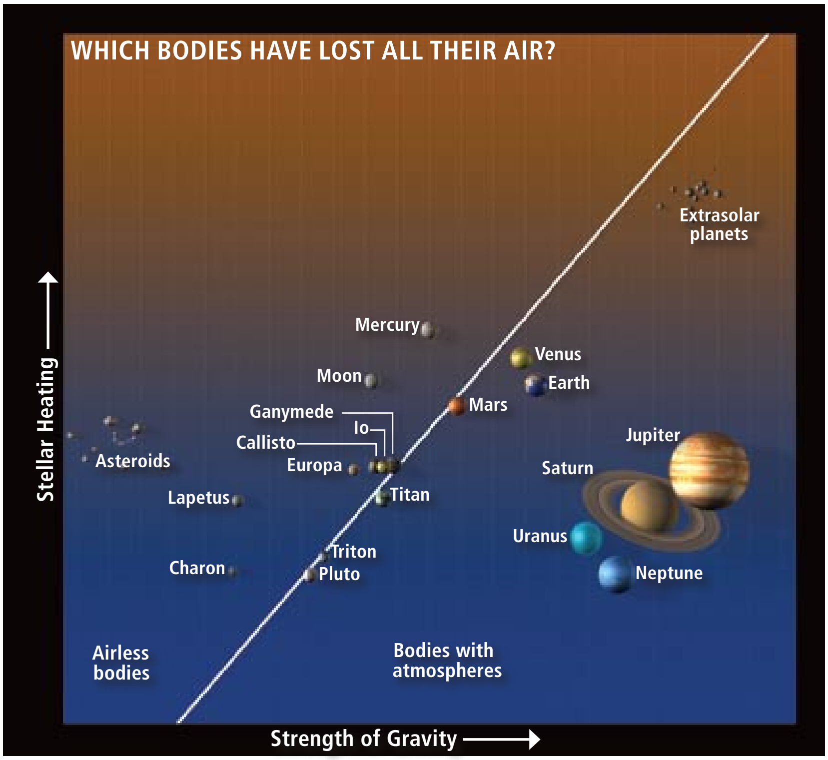
[ESCAPE MECHANISM #1]

# PLANETARY TEAKETTLE

**One major cause of air loss is solar heating. Heat can drive out air in one of two ways.**

**AIR EVAPORATES MOLECULE BY MOLECULE**
In an atmosphere's uppermost layer, or exosphere, nothing stops the fastest-moving atoms and molecules from flying off into space. This process, known as Jeans escape, accounts for much of the leakage of hydrogen from our planet.

**HEATED AIR FLOWS OUT IN A WIND**
Air heated by sunlight rises, accelerates and attains escape velocity. This process, known as hydrodynamic escape, was particularly important on early Earth and Venus—in fact, it may be why Venus became what it is today.


**EVIDENCE FOR THERMAL ESCAPE** comes from considering which planets and satellites have atmospheres and which do not. The deciding factor appears to be the strength of stellar heating (*vertical axis*) relative to the strength of a body's gravity (*horizontal axis*). Airless worlds have strong heating and weak gravity (*left of line*). Bodies with atmospheres have weak heating and strong gravity (*right of line*).

process prevails; for others, such as comets, the latter dominates. Even a body the size of Earth can heat up quickly if absorption and radiation get out of balance, and its atmosphere—which typically has very little mass compared with the rest of the planet—can slough off in a cosmic instant. Our solar system is littered with airless bodies, and thermal escape seems to be a common culprit. Airless bodies stand out as those where solar heating exceeds a certain threshold, which depends on the strength of the body's gravity [*see illustration above*].

Thermal escape occurs in two ways. In the first, called Jeans escape, after James Jeans, the English astronomer who described it in the early 20th century, air literally evaporates atom by atom, molecule by molecule, off the top of the atmosphere. At lower altitudes, collisions confine particles, but above a certain altitude, known as the exobase, which on Earth is about 500 kilometers above the surface, air is so tenuous that gas particles hardly ever collide. Nothing stops an atom or molecule with sufficient velocity from flying away into space.

As the lightest gas, hydrogen is the one that most easily overcomes a planet's gravity. But first it must reach the exobase, and on Earth that is a slow process. Hydrogen-bearing molecules tend not to rise above the lowest layer of atmosphere: water vapor ($H_2O$) condenses out and rains back down, and methane ($CH_4$) is oxidized to form carbon dioxide ($CO_2$). Some water and methane molecules reach the stratosphere and decompose, releasing hydrogen, which slowly diffuses upward until it reaches the exobase. A small amount clearly makes it out because ultraviolet images reveal a halo of hydrogen atoms surrounding our planet [*see illustration on opposite page*].

The temperature at Earth's exobase oscillates but is typically about 1,000 kelvins, implying that hydrogen atoms have an average speed of five kilometers per second. That is less than Earth's escape velocity at that altitude, 10.8 kilometers per second, but the average conceals a wide range, so some hydrogen atoms still manage to break free of our planet's gravity. This loss of particles from the energetic tail of the speed distribution explains about 10 to 40 percent of Earth's hydrogen loss today. Jeans escape also partly explains why our moon is airless. Gases

GEORGE RETSECK (*illustration*); ALFRED T. KAMAJIAN (*graph*) released from the lunar surface easily evaporate off into space.

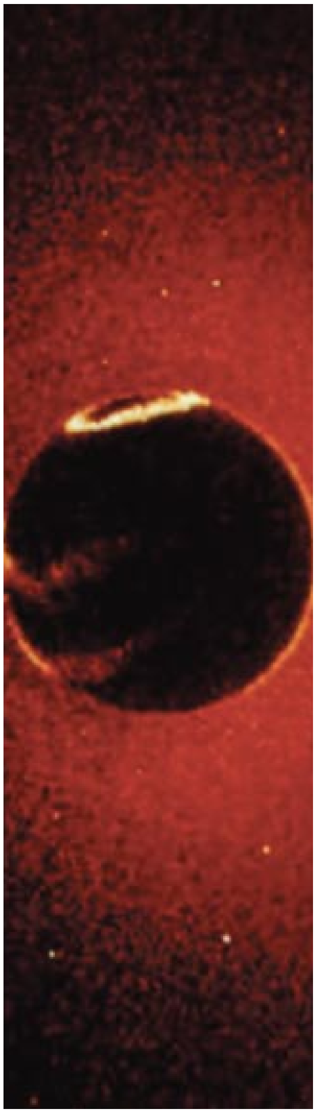
A second type of thermal escape is far more dramatic. Whereas Jeans escape occurs when a gas evaporates molecule by molecule, heated air can also flow en masse. The upper atmosphere can absorb ultraviolet sunlight, warm up and expand, pushing air upward. As the air rises, it accelerates smoothly through the speed of sound and then attains the escape velocity. This form of thermal escape is called hydrodynamic escape or, more evocatively, the planetary wind—the latter by analogy to the solar wind, the stream of charged particles blown from the sun into interplanetary space.

## Dust in the Wind

Atmospheres rich with hydrogen are the most vulnerable to hydrodynamic escape. As hydrogen flows outward, it can pick up and drag along heavier molecules and atoms with it. Much as the desert wind blows dust across an ocean and sand grains from dune to dune, while leaving cobbles and boulders behind, the hydrogen wind carries off molecules and atoms at a rate that diminishes with their weight. Thus, the present composition of an atmosphere can reveal whether this process has ever occurred.

In fact, astronomers have seen the telltale signs of hydrodynamic escape outside the solar system, on the Jupiter-like planet HD 209458b. Using the Hubble Space Telescope, Alfred Vidal-Madjar of the Paris Astrophysics Institute and his colleagues reported in 2003 that the planet has a puffed-up atmosphere of hydrogen. Subsequent measurements discovered carbon and oxygen in this inflated atmosphere. These atoms are too heavy to escape on their own, so they must have been dragged there by hydrogen. Hydrodynamic loss would also explain why astronomers find no large planets much closer to their stars than HD 209458b is. For planets that orbit within three million kilometers or so of their stars (about half the orbital radius of HD 209458b), hydrodynamic escape strips away the entire atmosphere within a few billion years, leaving behind only a scorched remnant.

This evidence for planetary winds lends credence to ideas put forth in the 1980s about hydrodynamic escape from ancient Venus, Earth and Mars. Three clues suggest this process once operated on these worlds. The first concerns noble gases. Were it not for escape, chemically unreactive gases such as neon or argon would remain in an atmosphere indefinitely. The abundances of their different isotopes would be similar to their original values, which in turn are similar to that of the sun, given their common origin in the solar nebula. Yet the abundances differ.



NASA/UNIVERSITY OF IOWA

**LEAKING HYDROGEN ATOMS give off a red glow in this ultraviolet image of Earth's night side, taken by NASA's Dynamic Explorer I satellite in 1982. Oxygen and nitrogen account for the band around the North Pole and the wisps in the tropics.**

Second, youthful stars are strong sources of ultraviolet light, and our sun was probably no exception. This radiation could have driven hydrodynamic escape.

Third, the early terrestrial planets may have had hydrogen-rich atmospheres. The hydrogen could have come from chemical reactions of water with iron, from nebular gases or from water molecules broken apart by solar ultraviolet radiation. In those primeval days, asteroids and comets hit more frequently, and whenever they smacked into an ocean, they filled the atmosphere with steam. Over thousands of years the steam condensed and rained back onto the surface, but Venus is close enough to the sun that water vapor may have persisted in the atmosphere, where solar radiation could break it down.

Under such conditions, hydrodynamic escape would readily operate. In the 1980s James F. Kasting, now at Pennsylvania State University, showed that hydrodynamic escape on Venus could have carried away an ocean's worth of hydrogen within a few tens of millions of years [see "How Climate Evolved on the Terrestrial Planets," by James F. Kasting, Owen B. Toon and James B. Pollack; Scientific American, February 1988]. Kasting and one of us (Zahnle) subsequently showed that escaping hydrogen would have dragged along much of the oxygen but left carbon dioxide behind. Without water to mediate the chemical reactions that turn carbon dioxide into carbonate minerals such as limestone, the carbon dioxide built up in the atmosphere and created the hellish Venus we see today.

To a lesser degree, Mars and Earth, too, appear to have suffered hydrodynamic losses. The telltale signature is a deficit of lighter isotopes, which are more easily lost. In the atmospheres of Earth and Mars, the ratio of neon 20 to neon 22 is 25 percent smaller than the solar ratio. On Mars, argon 36 is similarly depleted relative to argon 38. Even the isotopes of xenon—the heaviest gas in Earth's atmosphere apart from pollutants—show the imprint of hydrodynamic escape. If hydrodynamic escape were vigorous enough to sweep up xenon, why did it not sweep up everything else in the atmosphere along with it? To solve this puzzle, we may need to construct a different history for xenon than for the other gases now in the atmosphere.

Hydrodynamic escape may have stripped Titan of much of its air, too. When it descended through Titan's atmosphere in 2005, the European Space Agency's Huygens probe found that the ratio of nitrogen 14 to nitrogen 15 is 70 percent of that on Earth. That is a huge disparity given that the two isotopes differ only slightly in their tendency to escape. If Titan's atmosphere started with the same nitrogen isotopic composition as Earth's, it must have lost a huge amount of nitrogen—several times the substantial amount it currently has—to bring the ratio down to its present value. In short, Titan's atmosphere might once have been even thicker than it is today, which only heightens its mystery.

## Better Escaping through Chemistry

On some planets, including modern Earth, thermal escape is less important than nonthermal escape. In nonthermal escape, chemical reactions or particle-particle collisions catapult atoms to escape velocity. What nonthermal escape mechanisms have in common is that an atom or molecule reaches a very high velocity as the outcome of a single event that takes place above the exobase, so that bumping into something does not thwart the escapee. Many types of nonthermal escape involve ions. Ordinarily these charged particles are tethered to a planet by its magnetic field, either the global (internally generated) magnetic field—if there is one—or the localized fields induced by the passage of the solar wind. But they find ways to slip out.

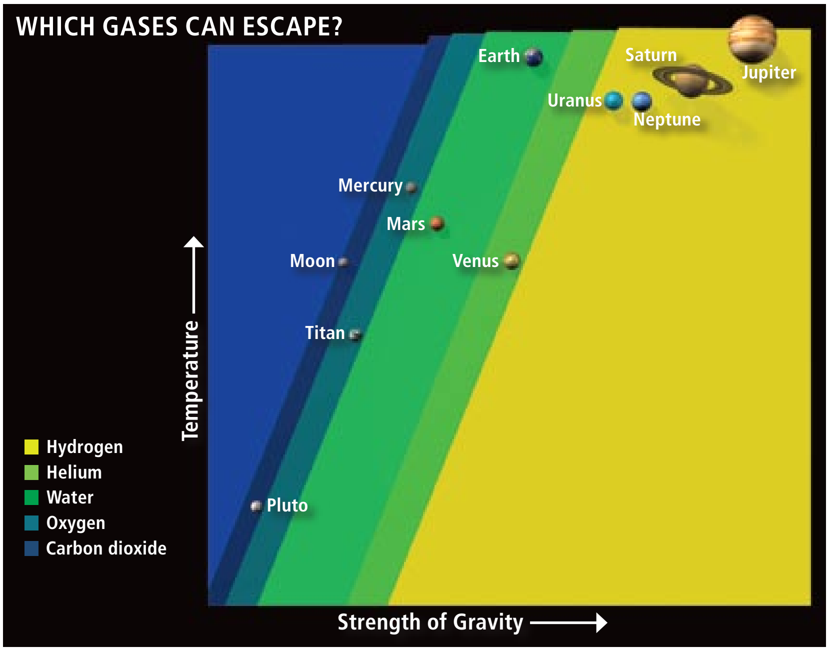
In one type of event, known as charge exchange, a fast hydrogen ion collides with a neutral hydrogen atom and captures its electron. The result is a fast neutral atom, which is immune to the magnetic field. This process accounts for 60 to 90 percent of the present loss of hydrogen from Earth and most of the hydrogen loss from Venus.

Another way out exploits a weak spot—dare we say a loophole—in the planet's magnetic trap. Most magnetic field lines loop from one magnetic pole to the other, but the widest field lines are dragged outward by the solar wind and do not loop back; they remain open to interplanetary space. Through this opening, ions can escape. To be sure, the ions must still overcome gravity, and only the lightest ions such as hydrogen and helium make it. The resulting stream of charged particles, called the polar wind (not to be confused with the planetary wind), accounts for 10 to 15 percent of Earth's hydrogen loss and almost its entire helium leak.

In some cases, these light ions can sweep up heavier ions with them. This process may explain the xenon puzzle: if the polar wind was more vigorous in the past, it could have dragged out xenon ions. One piece of evidence is that krypton does not have the same isotopic pattern as xenon does, even though it is a lighter gas and, all else being equal, ought to be more prone to escape. The difference is that krypton, unlike xenon, resists ionization, so even a strong polar wind would have left it unaffected.

A third nonthermal process known as photochemical escape operates on Mars and possibly on Titan. Oxygen, nitrogen and carbon monoxide molecules drift into the upper atmosphere, where solar radiation ionizes them. When the ionized molecules recombine with electrons or collide with one another, the energy released splits the molecules into atoms with enough speed to escape.

Mars, Titan and Venus lack global magnetic fields, so they are also vulnerable to a fourth nonthermal process known as sputtering. Without a planetary field to shield it, the upper atmosphere of each of these worlds is exposed to the full brunt of the solar wind. The wind picks up ions, which then undergo charge exchange and escape. Mars's atmosphere is enriched in heavy nitrogen and carbon isotopes, suggesting that it




**LIGHT GASES such as hydrogen are more footloose than heavier ones such as oxygen. Their susceptibility to Jeans escape depends on the temperature at the top of a body's atmosphere or, for airless bodies such as the moon, at its surface (*vertical axis*) and on the strength of its gravity (*horizontal axis*). If a body lies to the right of the line for a gas, it holds on to the gas; to the left, it loses the gas. For example, Mars loses hydrogen and helium, retains oxygen and carbon dioxide, and barely retains water.**

ALFRED T. KAMAJIAN (*graph*); GEORGE RETSECK (*illustration*)


**[THE AUTHORS]**

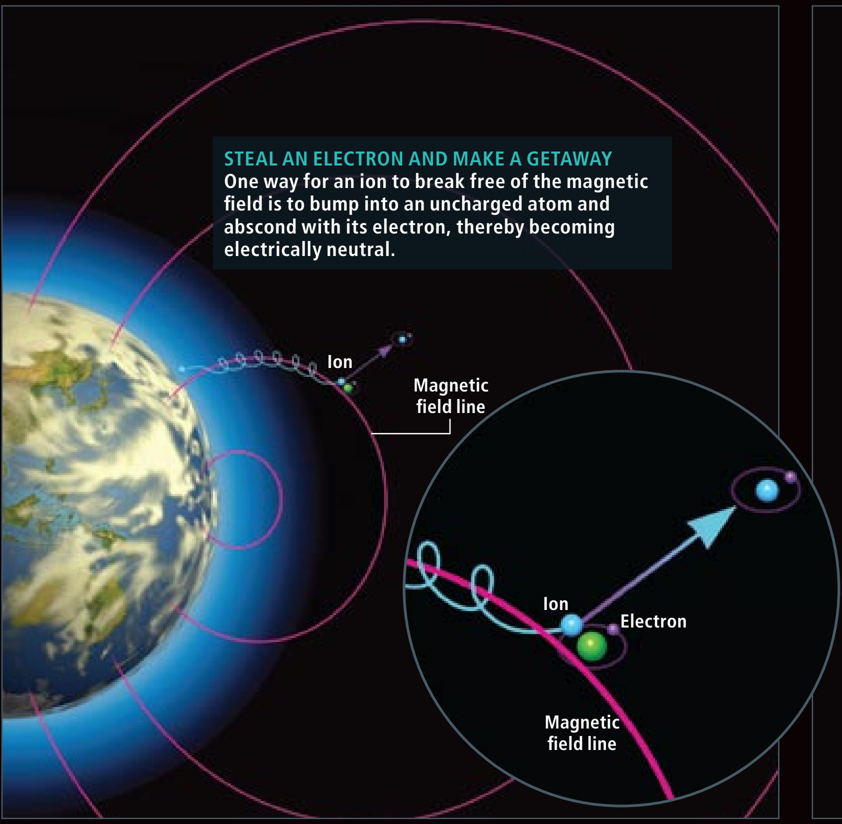
**Planetary scientist David C. Catling studies the coupled evolution of planetary surfaces and atmospheres. Formerly at the NASA Ames Research Center, he joined the faculty at the University of Washington in 2001. He is a co-investigator for NASA's Phoenix lander, which completed its mission last December. Kevin J. Zahnle has been a research scientist at the NASA Ames center since 1989. Even by the eclectic standards of planetary science, he has an unusually wide range of interests, from planetary interiors to surfaces to atmospheres. In 1996 Zahnle received the NASA Exceptional Achievement Medal for his work on the impact of Comet Shoemaker-Levy 9 into Jupiter.**

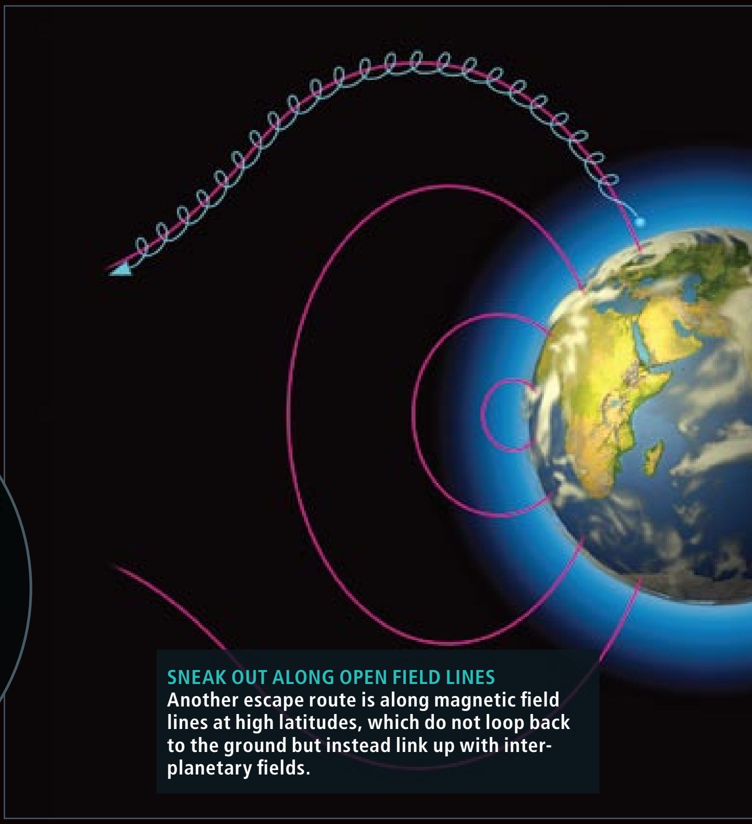
[ESCAPE MECHANISM #2]

# The Houdini Particles

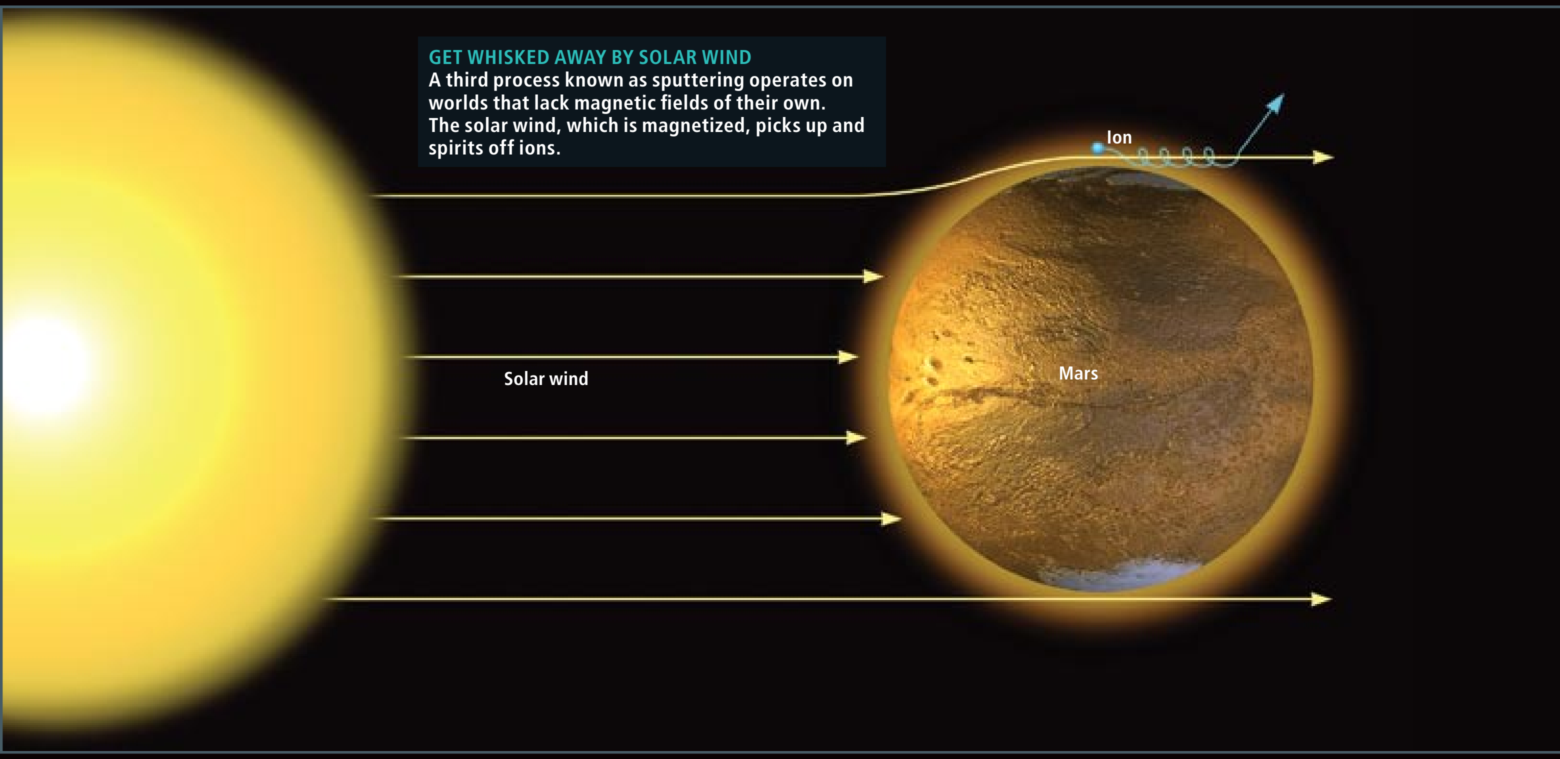
The second broad way that air escapes is through charged particle reactions. Electric fields readily accelerate ions to escape velocity. The planet's magnetic field traps them, but they have various tricks to slip out.




**STEAL AN ELECTRON AND MAKE A GETAWAY**
One way for an ion to break free of the magnetic field is to bump into an uncharged atom and abscond with its electron, thereby becoming electrically neutral.



**SNEAK OUT ALONG OPEN FIELD LINES**
Another escape route is along magnetic field lines at high latitudes, which do not loop back to the ground but instead link up with interplanetary fields.



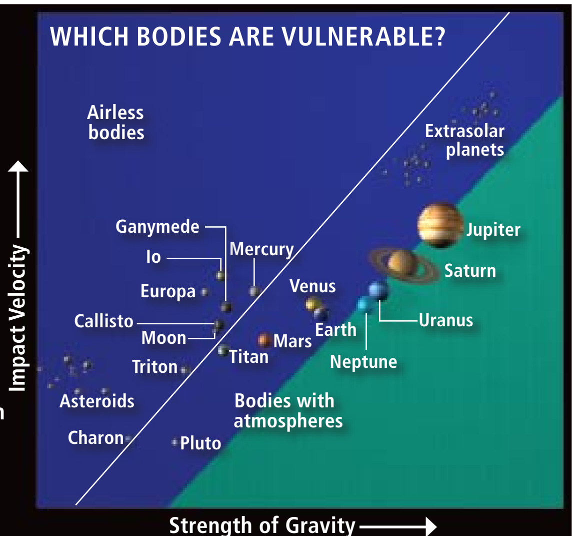

**GET WHISKED AWAY BY SOLAR WIND**
A third process known as sputtering operates on worlds that lack magnetic fields of their own. The solar wind, which is magnetized, picks up and spirits off ions.

[ESCAPE MECHANISM #3]

## AIR BLAST

When a comet or asteroid strikes a planet, it creates an enormous explosion that throws rock, water, dinosaurs and air into space.

**IMPACT EROSION is most severe when a body has weak gravity (*horizontal axis*) and when the incoming asteroids or comets smack at high speed (*vertical axis*). Airless bodies tend to lie toward the upper left of the graph, where erosion is worst. (The strength of gravity sets a minimum impact velocity, so the greenish area represents a range of velocities that can never arise in nature.)**




GEORGE RETSECK (*illustration*); ALFRED T. KAMAJIAN (*graph*)

has lost as much as 90 percent of an earlier atmosphere. Sputtering and photochemical escape are the most likely culprits. In 2013 NASA plans to launch the Mars Atmosphere and Volatile EvolutioN (MAVEN) mission to measure escaping ions and neutral atoms and reconstruct the planet's atmospheric history.

### Inescapable Consequences

Both thermal and nonthermal escape are like tiny trickles compared with the huge splash when comets or asteroids crash into planets. If projectiles are sufficiently big and fast, they vaporize both themselves and a similar mass of the surface. The ensuing hot gas plume can expand faster than the escape velocity and drive off the overlying air. The larger the impact energy, the wider the cone of atmosphere ejected. For the asteroid that killed off the dinosaurs 65 million years ago, the cone was about 80 degrees wide from the vertical and contained a hundred-thousandth of the atmosphere. An even more energetic impact can carry away the entire atmosphere above a plane that is tangent to the planet.

Another factor determining the width of the cone is the atmospheric density. The thinner the air, the greater the fraction of the atmosphere that gets lost. The implication is gloomy: once a vulnerable atmosphere starts wearing away, impact erosion becomes ever easier until the atmosphere vanishes altogether. Unfortunately, Mars spent its youth in a bad neighborhood near the asteroid belt and, being small, was especially susceptible. Given the expected size distribution of impactors early in a solar system's history, the planet should have been stripped of its entire atmosphere in less than 100 million years.

The large moons of Jupiter also live in a dangerous neighborhood—namely, deep in the giant planet's gravitational field, which accelerates incoming asteroids and comets. Impacts would have denuded these moons of any atmospheres they ever had. In contrast, Titan orbits comparatively far from Saturn, where impact velocities are slower and an atmosphere can survive.

In all these ways, escape accounts for much of the diversity of atmospheres, from the lack of air on Callisto and Ganymede to the absence of water on Venus. A more subtle consequence is that escape tends to oxidize planets, because hydrogen is lost more easily than oxygen. Hydrogen escape is the ultimate reason why Mars, Venus and even Earth are red. Most people do not think of Earth as a red planet, but much of the continental crust is red. Soil and vegetation hide this native hue. All three worlds started out the gray-black color of volcanic rock and reddened as the original minerals oxidized to iron oxides (similar to rust). To account for its color, Mars must have lost an ocean of water equivalent to a global layer meters to tens of meters deep.

On Earth, most researchers attribute the accumulation of oxygen 2.4 billion years ago to photosynthetic organisms, but in 2001 we suggested that the escape of hydrogen also played an important role. Microbes break apart water molecules in photosynthesis, and the hydrogen can pass like a baton from organic matter to methane and eventually reach space. The expected amount of hydrogen loss matches the net excess of oxidized material on Earth today.

Escape helps to solve the mystery of why

[WHICH MECHANISMS APPLY WHERE]

# A Litany of Losses

The three escape processes operate to different degrees on different planets and at different points in their history.

| BODY | PERIOD | KEY GASES LOST | THERMAL: JEANS ESCAPE | THERMAL: HYDRO-DYNAMIC | NONTHERMAL: CHARGE EXCHANGE | NONTHERMAL: POLAR WIND | NONTHERMAL: PHOTO-CHEMICAL | NONTHERMAL: SPUTTERING | IMPACT |
|---|---|---|---|---|---|---|---|---|---|
| Earth  | Now | Hydrogen | ✓ | | ✓ | ✓ | | | |
| | | Helium | | | ✓ | ✓ | | | |
| | Primordial | Hydrogen, neon | | ✓ | | | | | |
| Venus  | Now | Hydrogen, helium | | | ✓ | | | ✓ | |
| | Primordial | Hydrogen, oxygen | | ✓ | | | | | |
| Mars  | Now | Hydrogen | ✓ | | | | | | |
| | | Carbon, oxygen, nitrogen, argon | | | | | ✓ | ✓ | |
| | Primordial | All gases | | | | | | | ✓ |
| | | Hydrogen, carbon dioxide | | ✓ | | | | | |
| Jupiter's satellites  | Primordial | All gases | | ✓ | | | | | ✓ |
| Titan  | Now | Hydrogen | ✓ | | | | | ✓ | |
| | | Methane, nitrogen | | ? | | | | ✓ | ✓ |
| | Primordial | Hydrogen, methane, nitrogen | | ✓ | | | | | |
| Pluto  | Now | Hydrogen, methane, nitrogen | | ? | | | | | |
| HD 209458b | Now | Hydrogen, carbon, oxygen | | ✓ | | | | | |

ALFRED T. KAMAJIAN (*icons*)

Mars has such a thin atmosphere. Scientists have long hypothesized that chemical reactions among water, carbon dioxide and rock turned the original thick atmosphere into carbonate minerals. The carbonates were never recycled back into carbon dioxide gas because Mars, being so small, cooled quickly and its volcanoes stopped erupting. The trouble with this scenario is that spacecraft have so far found only a single small area on Mars with carbonate rock, and this outcrop probably formed in warm subsurface waters. Moreover, the carbonate theory offers no explanation for why Mars has so little nitrogen or noble gases. Escape provides a better answer. The atmosphere did not get locked away as rock; it dissipated into space.

A nagging problem is that impact erosion ought to have removed Mars's atmosphere altogether. What stopped it? One answer is simple chance. Large impacts are inherently rare, and their frequency fell off rapidly about 3.8 billion years ago, so Mars may have been spared the final devastating blow. A large impact of an icy asteroid or comet could have deposited more volatiles than subsequent impacts could remove. Alternatively, remnants of Mars's atmosphere may have survived underground and leaked out after the bombardment had subsided.

Although Earth seems comparatively unscathed by escape, that will change. Today hydrogen escape is limited to a trickle because the principal hydrogen-bearing gas, water vapor, condenses in the lower atmosphere and rains back to the surface. But our sun is slowly brightening at about 10 percent every billion years. That is imperceptibly slow on a human timescale but will be devastating over geologic time. As the sun brightens and our atmosphere warms, the atmosphere will get wetter, and the trickle of hydrogen escape will become a torrent.

This process is expected to become important when the sun is 10 percent brighter—that is, in a billion years—and it will take another billion years or so to desiccate our planet's oceans. Earth will become a desert planet, with at most a shrunken polar cap and only traces of precious liquid. After another two billion years, the sun will beat down on our planet so mercilessly even the polar oases will fail, the last liquid water will evaporate and the greenhouse effect will grow strong enough to melt rock. Earth will have followed Venus into a barren lifelessness. ■

## MORE TO EXPLORE


**Origins of Atmospheres.** K. J. Zahnle in *Origins*. Edited by C. E. Woodward, J. M. Shull and H. A. Thronson. Astronomical Society of the Pacific Conference Series, Vol. 148, 1998.

**An Extended Upper Atmosphere around the Extrasolar Planet HD209458b.** Alfred Vidal-Madjar et al. in *Nature*, Vol. 422, pages 143–146; March 13, 2003.

**Planetary Atmospheres and Life.** D. C. Catling and J. F. Kasting in *Planets and Life: The Emerging Science of Astrobiology.* Edited by W. T. Sullivan and J. A. Baross. Cambridge University Press, 2007.

# WHAT MAKES US HUMAN?

Comparisons of the genomes of humans and chimpanzees are revealing those rare stretches of DNA that are ours alone

By Katherine S. Pollard

Six years ago I jumped at an opportunity to join the international team that was identifying the sequence of DNA bases, or "letters," in the genome of the common chimpanzee (*Pan troglodytes*). As a biostatistician with a long-standing interest in human origins, I was eager to line up the human DNA sequence next to that of our closest living relative and take stock. A humbling truth emerged: our DNA blueprints are nearly 99 percent identical to theirs. That is, of the three billion letters that make up the human genome, only 15 million of them—less than 1 percent—have changed in the six million years or so since the human and chimp lineages diverged.

Evolutionary theory holds that the vast majority of these changes had little or no effect on our biology. But somewhere among those roughly 15 million bases lay the differences that made us human. I was determined to find them. Since then, I and others have made tantalizing progress in identifying a number of DNA sequences that set us apart from chimps.

## An Early Surprise

Despite accounting for just a small percentage of the human genome, millions of bases are still a vast territory to search. To facilitate the hunt, I wrote a computer program that would scan the human genome for the pieces of DNA that have changed the most since humans and chimps split from a common ancestor. Because most random genetic mutations neither benefit nor harm an organism, they accumulate at a steady rate that reflects the amount of time that has passed since two living species had a common forebear (this rate of change is often spoken of as the "ticking of the molecular clock"). Acceleration in that rate of change in some part of the genome, in contrast, is a hallmark of positive selection, in which mutations that help an organism survive and reproduce are more likely to be passed on to future generations. In other words, those parts of the code that have undergone the most modification since the chimp-human split are the sequences that most likely shaped humankind.

In November 2004, after months of debugging and optimizing my program to run on a massive computer cluster at the University of California, Santa Cruz, I finally ended up with a file that contained a ranked list of these rapidly evolving sequences. With my mentor David Haussler leaning over my shoulder, I looked at the top hit, a stretch of 118 bases that together became known as human accelerated region 1 (HAR1). Using the U.C. Santa Cruz genome browser, a visualization tool that annotates the

**KEY CONCEPTS**

- Chimpanzees are the closest living relatives of humans and share nearly 99 percent of our DNA.
- Efforts to identify those regions of the human genome that have changed the most since chimps and humans diverged from a common ancestor have helped pinpoint the DNA sequences that make us human.
- The findings have also provided vital insights into how chimps and humans can differ so profoundly, despite having nearly identical DNA blueprints.

*—The Editors*

**THE 1 PERCENT DIFFERENCE: Humans are distinct from chimpanzees in a number of important respects, despite sharing nearly 99 percent of their DNA. New analyses are revealing which parts of the genome set our species apart.**

JAMES BALOG *Getty Images*

human genome with information from public databases, I zoomed in on HAR1. The browser showed the HAR1 sequences of a human, chimp, mouse, rat and chicken—all of the vertebrate species whose genomes had been decoded by then. It also revealed that previous large-scale screening experiments had detected HAR1 activity in two samples of human brain cells, although no scientist had named or studied the sequence yet. We yelled, "Awesome!" in unison when we saw that HAR1 might be part of a gene new to science that is active in the brain.

We had hit the jackpot. The human brain is well known to differ considerably from the chimpanzee brain in terms of size, organization and complexity, among other traits. Yet the developmental and evolutionary mechanisms underlying the characteristics that set the human brain apart are poorly understood. HAR1 had the potential to illuminate this most mysterious aspect of human biology.

We spent the next year finding out all we could about the evolutionary history of HAR1 by comparing this region of the genome in various species, including 12 more vertebrates that were sequenced during that time. It turns out that until humans came along, HAR1 evolved extremely slowly. In chickens and chimps—whose lineages diverged some 300 million years ago—only two of the 118 bases differ, compared with 18 differences between humans and chimps, whose lineages diverged far more recently. The fact that HAR1 was essentially frozen in time through hundreds of millions of years indicates that it does something very important; that it then underwent abrupt revision in humans suggests that this function was significantly modified in our lineage.

A critical clue to the function of HAR1 in the brain emerged in 2005, after my collaborator Pierre Vanderhaeghen of the Free University of Brussels obtained a vial of HAR1 copies from our laboratory during a visit to Santa Cruz. He used these DNA sequences to design a fluorescent molecular tag that would light up when HAR1 was activated in living cells—that is, copied from DNA into RNA. When typical genes are switched on in a cell, the cell first makes a mobile messenger RNA copy and then uses the RNA as a template for synthesizing some needed protein. The labeling revealed that HAR1 is active in a type of neuron that plays a key role in the pattern and layout of the developing cerebral cortex, the wrinkled outermost brain layer. When things go wrong in these neurons, the result may be a severe, often deadly, congenital disorder known as lissencephaly (“smooth brain”), in which the cortex lacks its characteristic folds and exhibits a markedly reduced surface area. Malfunctions in these same neurons are also linked to the onset of schizophrenia in adulthood.

HAR1 is thus active at the right time and place to be instrumental in the formation of a healthy cortex. (Other evidence suggests that it may additionally play a role in sperm production.) But exactly how this piece of the genetic code affects cortex development is a mystery my colleagues and I are still trying to solve. We are eager to do so: HAR1’s recent burst of substitutions may have altered our brains significantly.

Beyond having a remarkable evolutionary history, HAR1 is special because it does not encode a protein. For decades, molecular biology research focused almost exclusively on genes that specify proteins, the basic building blocks of cells. But thanks to the Human Genome Project, which sequenced our own genome, scientists now know that protein-coding genes make up just 1.5 percent of our DNA. The other 98.5 percent—sometimes referred to as junk DNA—contains regulatory sequences that tell other genes when to turn on and off and genes encoding RNA that does not get translated into a protein, as well as a lot of DNA having purposes scientists are only beginning to understand.

Based on patterns in the HAR1 sequence, we predicted that HAR1 encodes RNA—a hunch that Sofie Salama, Haller Igel and Manuel Ares, all at U.C. Santa Cruz, subsequently confirmed in 2006 through lab experiments. In fact, it turns out that human HAR1 resides in two overlapping genes. The shared HAR1 sequence gives rise to an entirely new type of RNA structure, adding to the six known classes of RNA genes. These six major groups encompass more than 1,000 different families of RNA genes, each one distinguished by the structure and function of the encoded RNA in the cell. HAR1 is also the first documented example of an RNA-encoding sequence that appears to have undergone positive selection.

It might seem surprising that no one paid attention to these amazing 118 bases of the human genome earlier. But in the absence of technology for readily comparing whole genomes, researchers had no way of knowing that HAR1 was more than just another piece of junk DNA.

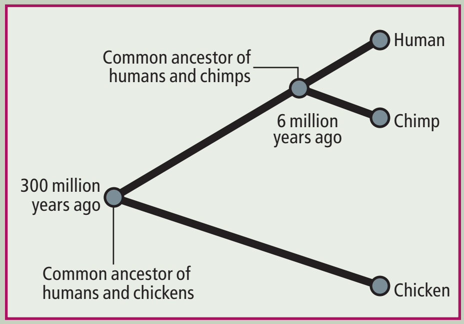
## Language Clues

Whole-genome comparisons in other species have also provided another crucial insight into why humans and chimps can be so different despite being much alike in their genomes. In recent years the genomes of thousands of species (mostly microbes) have been sequenced. It turns out that where DNA substitutions occur

[EXPERIMENT]

# SCANNING THE GENOME

To find the parts of our genome that make us human, the author wrote a computer program that searched for the DNA sequences that have changed the most since humans and chimpanzees diverged from their last common ancestor. Topping the list was a 118-letter snippet of code known as human accelerated region 1 (HAR1). This region of the genome changed very little for most of vertebrate evolution, with chimp and chicken sequences differing by just two letters. Human and chimp HAR1s, however, differ by 18 letters, suggesting that HAR1 acquired an important new function in humans.




| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T | G | A | A | A | **C** | G | G | A | G | G | A | G | A | **C** | **G** | T | T | A | C |
| A | G | C | A | A | **C** | **G** | T | **G** | T | C | A | **G** | C | T | G | A | A | A | T |
| **G** | A | T | **G** | G | G | **C** | G | T | A | G | A | C | **G** | C | A | **C** | G | T | C |
| A | G | C | **G** | G | **C** | G | G | A | A | A | T | **G** | G | T | T | T | C | T | A |
| T | C | A | A | A | A | T | **G** | A | A | A | G | T | **G** | T | T | T | A | G | A |
| G | A | T | T | T | C | C | T | C | A | A | **G** | T | T | T | C | A | | | |

Changes in human sequence relative to that of the chimp

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T | G | A | A | A | T | G | G | A | G | G | A | G | A | A | A | T | T | A | C |
| A | G | C | A | A | T | T | T | A | T | C | A | A | C | T | G | A | A | A | T |
| T | A | T | A | G | G | T | G | T | A | G | A | C | A | C | A | T | G | T | C |
| A | G | C | A | G | T | **G** | G | A | A | A | **T** | A | G | T | T | T | C | T | A |
| T | C | A | A | A | A | T | T | A | A | A | G | T | A | T | T | T | A | G | A |
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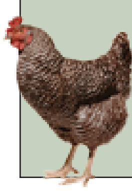
Changes in chimp sequence relative to that of the chicken



| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T | G | A | A | A | T | G | G | A | G | G | A | G | A | A | A | T | T | A | C |
| A | G | C | A | A | T | T | T | A | T | C | A | A | C | T | G | A | A | A | T |
| T | A | T | A | G | G | T | G | T | A | G | A | C | A | C | A | T | G | T | C |
| A | G | C | A | G | T | A | G | A | A | A | C | A | G | T | T | T | C | T | A |
| T | C | A | A | A | A | T | T | A | A | A | G | T | A | T | T | T | A | G | A |
| G | A | T | T | T | C | C | T | C | A | A | A | T | T | T | C | A | | | |

GETTY IMAGES *(man)*; DORLING KINDERSLEY *Getty Images (chimp)*; GK AND VIKKI HART *Getty Images (chicken)* in the genome—rather than how many changes arise overall—can matter a great deal. In other words, you do not need to change very much of the genome to make a new species. The way to evolve a human from a chimp-human ancestor is not to speed the ticking of the molecular clock as a whole. Rather the secret is to have rapid change occur in sites where those changes make an important difference in an organism's functioning.

HAR1 is certainly such a place. So, too, is the *FOXP2* gene, which contains another of the fast-changing sequences I identified and is known to be involved in speech. Its role in speech was discovered by researchers at the University of Oxford in England, who reported in 2001 that people with mutations in the gene are unable to make certain subtle, high-speed facial movements needed for normal human speech, even though they possess the cognitive ability to process language. The typical human sequence displays several differences from the chimp's: two base substitutions that altered its protein product and many other substitutions that may have led to shifts affecting how, when and where the protein is used in the human body.

A recent finding has shed some light on when the speech-enabling version of *FOXP2* appeared in hominids: in 2007 scientists at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, sequenced *FOXP2* extracted from a Neandertal fossil and found that these extinct humans had the modern human version of the gene, perhaps permitting them to enunciate as we do. Current estimates for when the Neandertal and modern human lineages split suggest that the new form of *FOXP2* must have emerged at least half a million years ago. Most of what distinguishes human language from vocal communication in other species, however, comes not from physical means but cognitive ability, which is often correlated with brain size. Primates generally have a larger brain than would be expected from their body size. But human brain volume has more than tripled since the chimp-human ancestor—a growth spurt that genetics researchers have only begun to unravel.

One of the best-studied examples of a gene linked to brain size in humans and other animals is *ASPM*. Genetic studies of people with a condition known as microcephaly, in which the brain is reduced by up to 70 percent, uncovered the role of *ASPM* and three other genes—*MCPH1, CDK5RAP2* and *CENPJ*—in controlling brain size. More recently, researchers at the University of Chicago and the University of Michigan at Ann Arbor have shown that *ASPM* experienced several bursts of change over the course of primate evolution, a pattern indicative of positive selection. At least one of these bursts occurred in the human lineage since it diverged from that of chimps and thus was potentially instrumental in the evolution of our large brains.

Other parts of the genome may have influenced the metamorphosis of the human brain less directly. The computer scan that identified HAR1 also found 201 other human accelerated regions, most of which do not encode proteins or even RNA. (A related study conducted at the Wellcome Trust Sanger Institute in Cambridge, England, detected many of the same HARs.) Instead they appear to be regulatory sequences that tell nearby genes when to turn on and off. Amazingly, more than half of the genes located near HARs are involved in brain development and function. And, as is true of *FOXP2*, the products of many of these genes go on to regulate other genes. Thus, even though HARs make up a minute portion of the genome, changes in these regions could have profoundly altered the human brain by influencing the activity of whole networks of genes.

**You do not need to change very much of the genome to make a new species.**

## Beyond the Brain

Although much genetic research has focused on elucidating the evolution of our sophisticated brain, investigators have also been piecing together how other unique aspects of the human body came to be. HAR2, a gene regulatory region and the second most accelerated site on my list, is a case in point. In 2008 researchers at Lawrence Berkeley National Laboratory showed that specific base differences in the human version of HAR2 (also known as HACNS1), relative to the version in nonhuman primates, allow this DNA sequence to drive gene activity in the wrist and thumb during fetal development, whereas the ancestral version in other primates cannot. This finding is particularly provocative because it could underpin morphological changes in the human hand that permitted the dexterity needed to manufacture and use complex tools.

Aside from undergoing changes in form, our ancestors also underwent behavioral and physiological shifts that helped them adapt to altered circumstances and migrate into new environments. For example, the conquest of fire more than a million years ago and the agricultural

**[THE AUTHOR]**

COURTESY OF MICHAEL MCCOLL

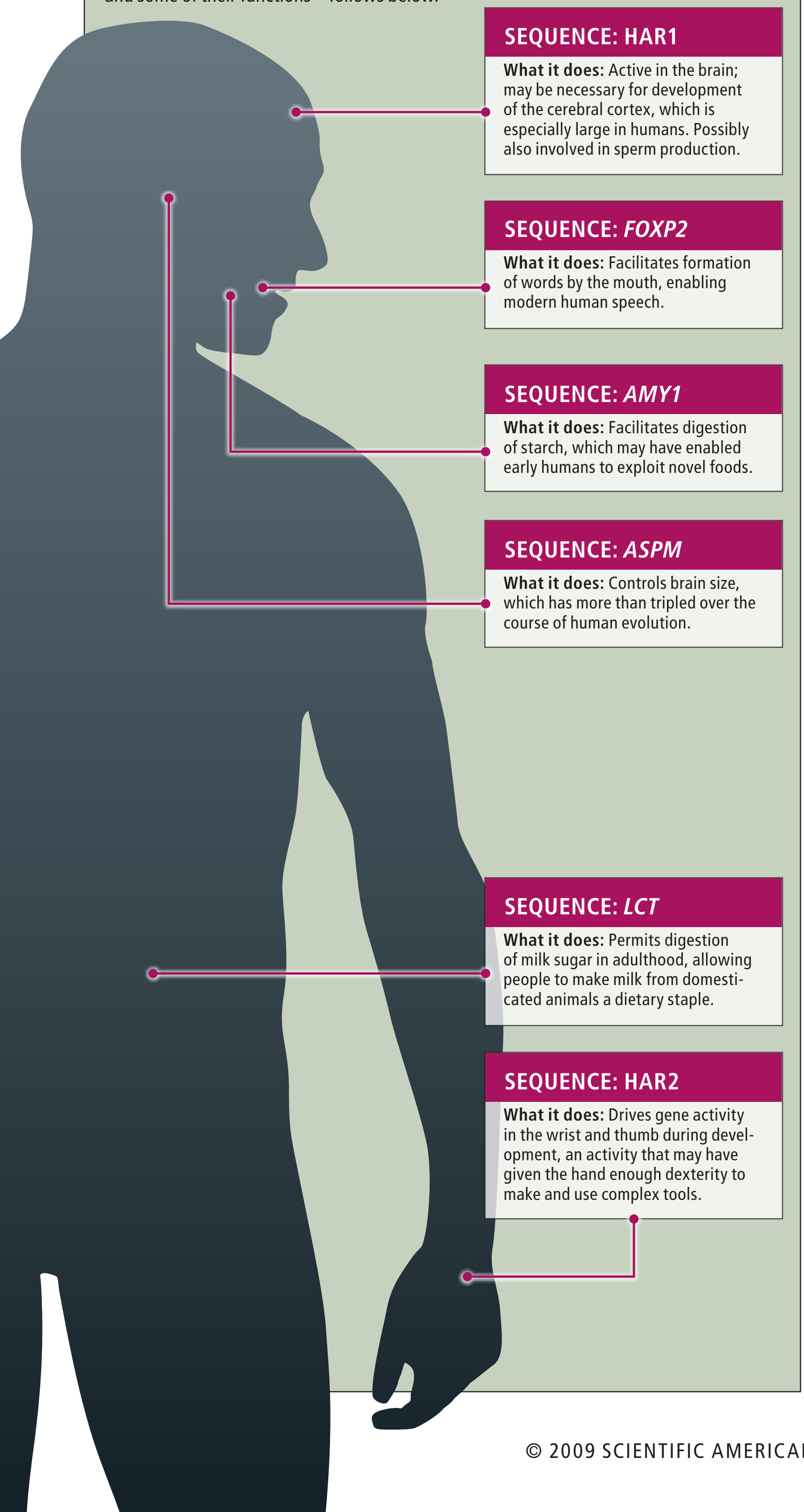
**Katherine S. Pollard** is a biostatistician at the University of California, San Francisco. In 2003, after completing a Ph.D. and postdoctoral research at U.C. Berkeley, she began a comparative genomics fellowship at U.C. Santa Cruz, during which she participated in the sequencing of the chimpanzee genome. Pollard used this sequence to identify the fastest-evolving regions of the human genome. A recipient in 2008 of a Sloan Research Fellowship in Computational and Evolutionary Molecular Biology, she recently began studying the evolution of microbes that live in the human body.

[FINDINGS]

## DISTINCTIVE DNA

Efforts to uncover uniquely human DNA have yielded a number of sequences that are distinctive in humans as compared with chimpanzees. A partial list of these sequences—and some of their functions—follows below.




MELISSA THOMAS

revolution about 10,000 years ago made foods high in starch more accessible. But cultural shifts alone were not sufficient to exploit these calorie-rich comestibles. Our predecessors had to adapt genetically to them.

Changes in the gene *AMY1*, which encodes salivary amylase, an enzyme involved in digesting starch, constitute one well-known adaptation of this kind. The mammalian genome contains multiple copies of this gene, with the number of copies varying between species and even between individual humans. But overall, compared with other primates, humans have an especially large number of *AMY1* copies. In 2007 geneticists at Arizona State University showed that individuals carrying more copies of *AMY1* have more amylase in their saliva, thereby allowing them to digest more starch. The evolution of *AMY1* thus appears to involve both the number of copies of the gene and the specific changes in its DNA sequence.

Another famous example of dietary adaptation involves the gene for lactase (*LCT*), an enzyme that allows mammals to digest the carbohydrate lactose, also known as milk sugar. In most species, only nursing infants can process lactose. But around 9,000 years ago—very recently, in evolutionary terms—changes in the human genome produced versions of *LCT* that allowed adults to digest lactose. Modified *LCT* evolved independently in European and African populations, enabling carriers to digest milk from domesticated animals. Today adult descendants of these ancient herders are much more likely to tolerate lactose in their diets than are adults from other parts of the world, including Asia and Latin America, many of whom are lactose-intolerant as a result of having the ancestral primate version of the gene.

*LCT* is not the only gene known to be evolving in humans right now. The chimp genome project identified 15 others in the process of shifting away from a version that was perfectly normal in our ape ancestors and that works fine in other mammals but, in that old form, is associated with diseases such as Alzheimer's and cancer in modern humans. Several of these disorders afflict humans alone or occur at higher rates in humans than in other primates. Scientists are currently researching the functions of the genes involved and are attempting to establish why the ancestral versions of these genes became maladaptive in us. These studies could help medical practitioners identify those patients who have a higher chance of getting one of these life-threatening diseases, in hopes of helping them stave off illness. The studies may also help researchers identify and develop new treatments.

**BRAIN SHAPERS:** Changes to certain genome sequences can have dramatic effects on the brain. Mutation of the *ASPM* gene, for example, leads to markedly reduced brain size (*middle*) compared with a normal brain (*top*), suggesting that this gene played a key role in the evolution of large brain size in humans. Malfunctions in the neurons in which HAR1 is active during development, meanwhile, can lead to a severe disorder in which the brain's cerebral cortex fails to fold properly (*bottom*), hinting that HAR1 is essential for the formation of a healthy cortex.

COURTESY OF GANESHWARAN H. MOCHIDA, C. GEOFFREY WOODS AND CHRISTOPHER A. WALSH (*top and middle*); COURTESY OF GAVIN UDSTUEN *University of Cincinnati* (*bottom*)

## With the Good Comes the Bad

Battling disease so we can pass our genes along to future generations has been a constant refrain in the evolution of humans, as in all species. Nowhere is this struggle more evident than in the immune system. When researchers examine the human genome for evidence of positive selection, the top candidates are frequently involved in immunity. It is not surprising that evolution tinkers so much with these genes: in the absence of antibiotics and vaccines, the most likely obstacle to individuals passing along their genes would probably be a life-threatening infection that strikes before the end of their childbearing years. Further accelerating the evolution of the immune system is the constant adaptation of pathogens to our defenses, leading to an evolutionary arms race between microbes and hosts.

Records of these struggles are left in our DNA. This is particularly true for retroviruses, such as HIV, that survive and propagate by inserting their genetic material into our genomes. Human DNA is littered with copies of these short retroviral genomes, many from viruses that caused diseases millions of years ago and that may no longer circulate. Over time the retroviral sequences accumulate random mutations just as any other sequence does, so that the different copies are similar but not identical. By examining the amount of divergence among these copies, researchers can use molecular clock techniques to date the original retroviral infection. The scars of these ancient infections are also visible in the host immune system genes that constantly adapt to fight the ever evolving retroviruses.

PtERV1 is one such relic virus. In modern humans, a protein called TRIM5α works to prevent PtERV1 and related retroviruses from replicating. Genetic evidence suggests that a PtERV1 epidemic plagued ancient chimpanzees, gorillas and humans living in Africa about four million years ago. To figure out how different primates responded to PtERV1, in 2007 researchers at the Fred Hutchinson Cancer Research Center in Seattle used the many randomly mutated copies of PtERV1 in the chimpanzee genome to reconstruct the original PtERV1 sequence and re-create this ancient retrovirus. They then performed experiments to see how well the human and great ape versions of the *TRIM5*α gene could restrict the activity of the resurrected PtERV1 virus. Their results indicate that a single change in human *TRIM5*α most likely enabled our ancestors to fight PtERV1 infection more effectively than our primate cousins could. (Additional changes in human *TRIM5*α may have evolved in response to a related retrovirus.) Other primates have their own sets of changes in *TRIM5*α, probably reflecting retroviral battles that their predecessors won.

Defeating one type of retrovirus does not necessarily guarantee continued success against others, however. Although changes in human *TRIM5*α may have helped us survive PtERV1, these same shifts make it much harder for us to fight HIV. This finding is helping researchers to understand why HIV infection leads to AIDS in humans but not in nonhuman primates. Clearly, evolution can take one step forward and two steps back. Sometimes scientific research feels the same way. We have identified many exciting candidates for explaining the genetic basis of distinctive human traits. In most cases, though, we know only the basics about the function of these genome sequences. The gaps in our knowledge are especially large for regions such as HAR1 and HAR2 that do not encode proteins.

These rapidly evolving, uniquely human sequences do point to a way forward. The story of what made us human is probably not going to focus on changes in our protein building blocks but rather on how evolution assembled these blocks in new ways by changing when and where in the body different genes turn on and off. Experimental and computational studies now under way in thousands of labs around the world promise to elucidate what is going on in the 98.5 percent of our genome that does not code for proteins. It is looking less and less like junk every day. ■

## ➡ MORE TO EXPLORE


**Mapping Human History: Discovering the Past through Our Genes.** Steve Olson. Houghton Mifflin, 2002.

**The Ancestor's Tale: A Pilgrimage to the Dawn of Evolution.** Richard Dawkins. Houghton Mifflin, 2004.

**Initial Sequence of the Chimpanzee Genome and Comparison with the Human Genome.** The Chimpanzee Sequencing and Analysis Consortium in *Nature*, Vol. 437, pages 69–87; September 1, 2005.

University of California, Santa Cruz, Genome Bioinformatics Web site: **http://genome.ucsc.edu**

# COULD FOOD SHORTAGES BRING DOWN CIVILIZATION?

**The biggest threat to global stability is the potential for food crises in poor countries to cause government collapse. Those crises are brought on by ever worsening environmental degradation**

BY LESTER R. BROWN

## KEY CONCEPTS

- Food scarcity and the resulting higher food prices are pushing poor countries into chaos.
- Such "failed states" can export disease, terrorism, illicit drugs, weapons and refugees.
- Water shortages, soil losses and rising temperatures from global warming are placing severe limits on food production.
- Without massive and rapid intervention to address these three environmental factors, the author argues, a series of government collapses could threaten the world order.

*—The Editors*

One of the toughest things for people to do is to anticipate sudden change. Typically we project the future by extrapolating from trends in the past. Much of the time this approach works well. But sometimes it fails spectacularly, and people are simply blindsided by events such as today's economic crisis.

For most of us, the idea that civilization itself could disintegrate probably seems preposterous. Who would not find it hard to think seriously about such a complete departure from what we expect of ordinary life? What evidence could make us heed a warning so dire—and how would we go about responding to it? We are so inured to a long list of highly unlikely catastrophes that we are virtually programmed to dismiss them all with a wave of the hand: Sure, our civilization might devolve into chaos—and Earth might collide with an asteroid, too!

For many years I have studied global agricultural, population, environmental and economic trends and their interactions. The combined effects of those trends and the political tensions they generate point to the breakdown of governments and societies. Yet I, too, have resisted the idea that food shortages could bring down not only individual governments but also our global civilization.

I can no longer ignore that risk. Our continuing failure to deal with the environmental declines that are undermining the world food economy—most important, falling water tables, eroding soils and rising temperatures—forces me to conclude that such a collapse is possible.

## The Problem of Failed States

Even a cursory look at the vital signs of our current world order lends unwelcome support to my conclusion. And those of us in the environmental field are well into our third decade of charting trends of environmental decline without seeing any significant effort to reverse a single one.

In six of the past nine years world grain production has fallen short of consumption, forcing a steady drawdown in stocks. When the 2008 harvest began, world carryover stocks of grain (the amount in the bin when the new harvest begins) were at 62 days of consumption, a near re-

PER-ANDERS PETTERSSON *Getty Images*

**CHILDREN CLAMOR** for food in the village of Dubie, Democratic Republic of the Congo. The photograph was taken in December 2005.

## FAILING STATES

**Every year the Fund for Peace and the Carnegie Endowment for International Peace jointly analyze and score countries on 12 social, economic, political and military indicators of national well-being. Here, ranked from worst to better according to their combined scores in 2007, are the 20 countries in the world that are closest to collapse:**

- Somalia
- Sudan
- Zimbabwe
- Chad
- Iraq
- Democratic Republic of the Congo
- Afghanistan
- Ivory Coast
- Pakistan
- Central African Republic
- Guinea
- Bangladesh
- Burma (Myanmar)
- Haiti
- North Korea
- Ethiopia
- Uganda
- Lebanon
- Nigeria
- Sri Lanka

*SOURCE: "The Failed States Index 2008," by the Fund for Peace and the Carnegie Endowment for International Peace, in* Foreign Policy; *July/August 2008*

cord low. In response, world grain prices in the spring and summer of last year climbed to the highest level ever.

As demand for food rises faster than supplies are growing, the resulting food-price inflation puts severe stress on the governments of countries already teetering on the edge of chaos. Unable to buy grain or grow their own, hungry people take to the streets. Indeed, even before the steep climb in grain prices in 2008, the number of failing states was expanding [*see sidebar at left*]. Many of their problems stem from a failure to slow the growth of their populations. But if the food situation continues to deteriorate, entire nations will break down at an ever increasing rate. We have entered a new era in geopolitics. In the 20th century the main threat to international security was superpower conflict; today it is failing states. It is not the concentration of power but its absence that puts us at risk.

States fail when national governments can no longer provide personal security, food security and basic social services such as education and health care. They often lose control of part or all of their territory. When governments lose their monopoly on power, law and order begin to disintegrate. After a point, countries can become so dangerous that food relief workers are no longer safe and their programs are halted; in Somalia and Afghanistan, deteriorating conditions have already put such programs in jeopardy.

Failing states are of international concern because they are a source of terrorists, drugs, weapons and refugees, threatening political stability everywhere. Somalia, number one on the 2008 list of failing states, has become a base for piracy. Iraq, number five, is a hotbed for terrorist training. Afghanistan, number seven, is the world's leading supplier of heroin. Following the massive genocide of 1994 in Rwanda, refugees from that troubled state, thousands of armed soldiers among them, helped to destabilize neighboring Democratic Republic of the Congo (number six).

Our global civilization depends on a functioning network of politically healthy nation-states to control the spread of infectious disease, to manage the international monetary system, to control international terrorism and to reach scores of other common goals. If the system for controlling infectious diseases—such as polio, SARS or avian flu—breaks down, humanity will be in trouble. Once states fail, no one assumes responsibility for their debt to outside lenders. If enough states disintegrate, their fall will threaten the stability of global civilization itself.

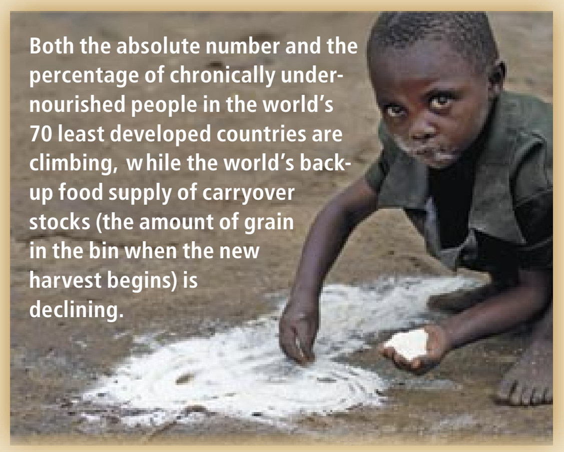
### A New Kind of Food Shortage

The surge in world grain prices in 2007 and 2008—and the threat they pose to food security—has a different, more troubling quality than the increases of the past. During the second half of the 20th century, grain prices rose dramatically several times. In 1972, for instance, the Soviets, recognizing their poor harvest early, quietly cornered the world wheat market. As a result, wheat prices elsewhere more than doubled, pulling rice and corn prices up with them. But this and other price shocks were event-driven—

YASUYOSHI CHIBA *Getty Images*

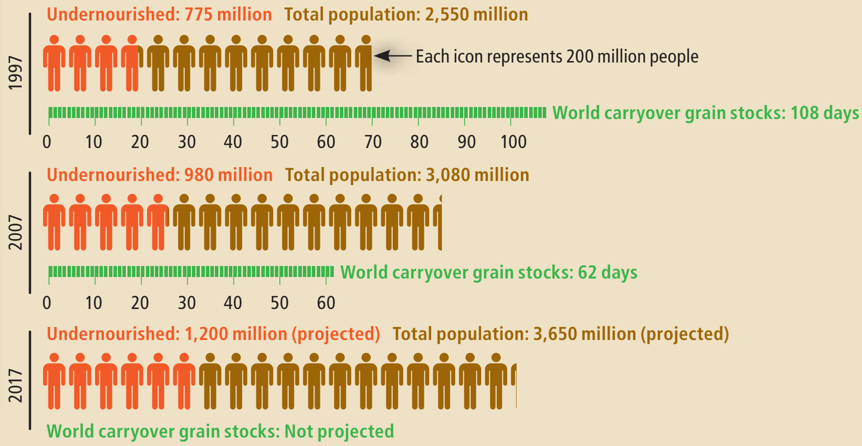
[FOOD STRESS ON THE RISE]

## Numbers That Go the Wrong Way



**Both the absolute number and the percentage of chronically undernourished people in the world's 70 least developed countries are climbing, while the world's backup food supply of carryover stocks (the amount of grain in the bin when the new harvest begins) is declining.**

**RISING HUNGER IN THE WORLD'S 70 LEAST DEVELOPED COUNTRIES**




*SOURCES: U.S. Department of Agriculture, 2008; U.S. Census Bureau* drought in the Soviet Union, a monsoon failure in India, crop-shrinking heat in the U.S. Corn Belt. And the rises were short-lived: prices typically returned to normal with the next harvest.

In contrast, the recent surge in world grain prices is trend-driven, making it unlikely to reverse without a reversal in the trends themselves. On the demand side, those trends include the ongoing addition of more than 70 million people a year; a growing number of people wanting to move up the food chain to consume highly grain-intensive livestock products [see "The Greenhouse Hamburger," by Nathan Fiala; Scientific American, February 2009]; and the massive diversion of U.S. grain to ethanol-fuel distilleries.

The extra demand for grain associated with rising affluence varies widely among countries. People in low-income countries where grain supplies 60 percent of calories, such as India, directly consume a bit more than a pound of grain a day. In affluent countries such as the U.S. and Canada, grain consumption per person is nearly four times that much, though perhaps 90 percent of it is consumed indirectly as meat, milk and eggs from grain-fed animals.

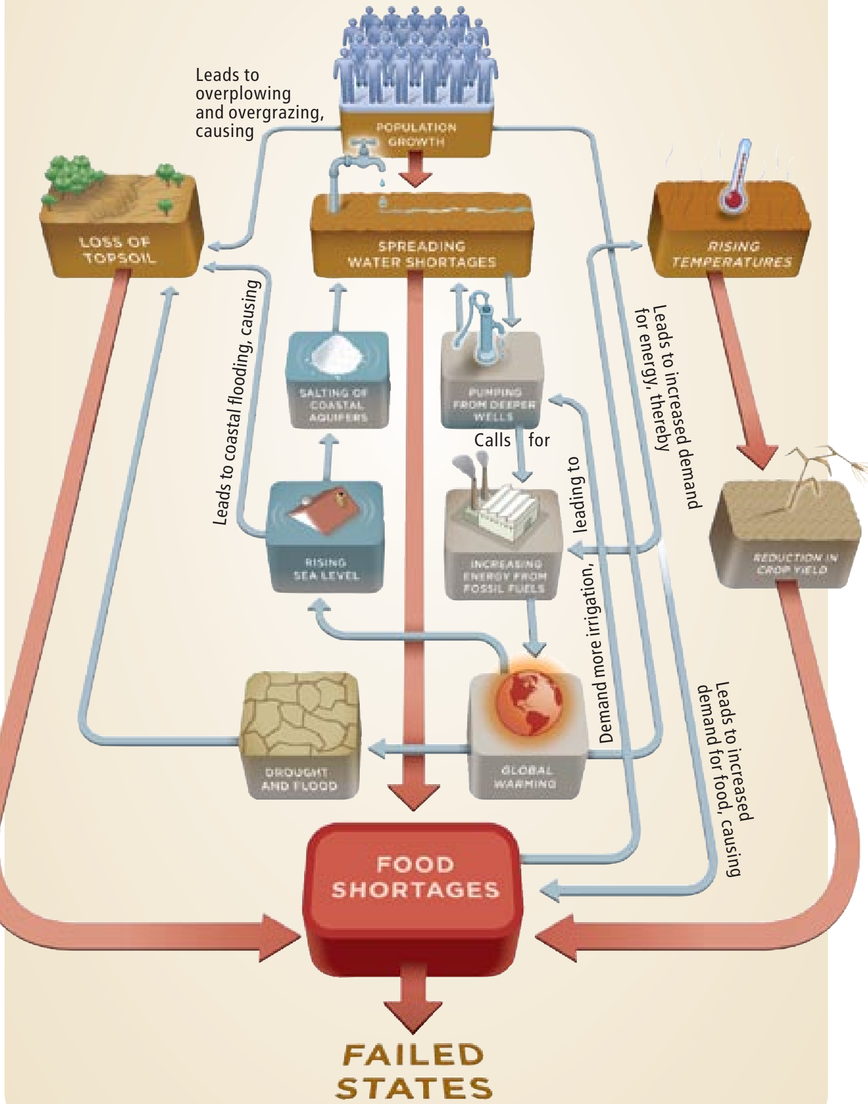
The potential for further grain consumption as incomes rise among low-income consumers is huge. But that potential pales beside the insatiable demand for crop-based automotive fuels. A fourth of this year's U.S. grain harvest—enough to feed 125 million Americans or half a billion Indians at current consumption levels—will go to fuel cars. Yet even if the entire U.S. grain harvest were diverted into making ethanol, it would meet at most 18 percent of U.S. automotive fuel needs. The grain required to fill a 25-gallon SUV tank with ethanol could feed one person for a year.

The recent merging of the food and energy economies implies that if the food value of grain is less than its fuel value, the market will move the grain into the energy economy. That double demand is leading to an epic competition between cars and people for the grain supply and to a political and moral issue of unprecedented dimensions. The U.S., in a misguided effort to reduce its dependence on foreign oil by substituting grain-based fuels, is generating global food insecurity on a scale not seen before.

[CAUSES AND EFFECTS]

## Key Factors in Food Shortages

The spreading scarcity of food is emerging as the central cause of state failure. Food shortages arise out of a tangled web of causes, effects and feedbacks whose interactions often intensify the effects of any one factor acting alone. Some of the most common factors are depicted in the diagram. According to the author, today's food shortages are not the result of one-time, weather-driven crop failures but rather of four critical long-term trends (*below*): rapid population growth, loss of topsoil, spreading water shortages and rising temperatures.




SAMUEL VELASCO 5W Infographics

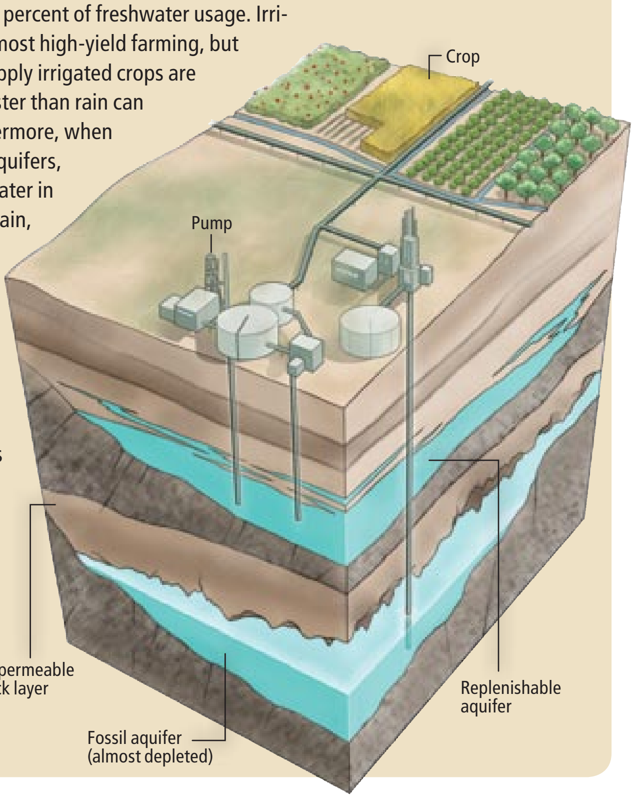
### Water Shortages Mean Food Shortages

What about supply? The three environmental trends I mentioned earlier—the shortage of freshwater, the loss of topsoil and the rising temperatures (and other effects) of global warming—are making it increasingly hard to expand the world's grain supply fast enough to keep up with demand. Of all those trends, however, the spread of water shortages poses the most immediate threat. The biggest challenge here is irrigation, which consumes 70 percent of the world's freshwater. Millions of irrigation wells in many countries are now pumping water out of under-

[FALLING WATER TABLES]

## Irrigation Can Lead to Severe Water Shortages

The greatest drain on supplies of freshwater is irrigation, which accounts for 70 percent of freshwater usage. Irrigation is essential to most high-yield farming, but many aquifers that supply irrigated crops are being drawn down faster than rain can recharge them. Furthermore, when farmers tap "fossil" aquifers, which store ancient water in rock impermeable to rain, they are mining a nonrenewable resource. Pumping from ever deeper wells is problematic in another way as well: it takes a lot of energy. In some states of India, half of the available electricity is used to pump water.

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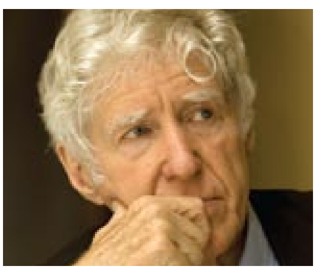


**Lester R. Brown, in the words of the *Washington Post,* is "one of the world's most influential thinkers." The *Telegraph* of Calcutta has called him "the guru of the environmental movement." Brown is founder of both the Worldwatch Institute (1974) and the Earth Policy Institute (2001), which he heads today. He has authored or coauthored 50 books; his most recent is *Plan B 3.0: Mobilizing to Save Civilization.* Brown is the recipient of many prizes and awards, including 24 honorary degrees and a MacArthur Fellowship.**

ground sources faster than rainfall can recharge them. The result is falling water tables in countries populated by half the world's people, including the three big grain producers—China, India and the U.S.

Usually aquifers are replenishable, but some of the most important ones are not: the "fossil" aquifers, so called because they store ancient water and are not recharged by precipitation. For these—including the vast Ogallala Aquifer that underlies the U.S. Great Plains, the Saudi aquifer and the deep aquifer under the North China Plain—depletion would spell the end of pumping. In arid regions such a loss could also bring an end to agriculture altogether.

In China the water table under the North China Plain, an area that produces more than half of the country's wheat and a third of its corn, is falling fast. Overpumping has used up most of the water in a shallow aquifer there, forcing well drillers to turn to the region's deep aquifer, which is not replenishable. A report by the World Bank foresees "catastrophic consequences for future generations" unless water use and supply can quickly be brought back into balance.

As water tables have fallen and irrigation wells have gone dry, China's wheat crop, the world's largest, has declined by 8 percent since it peaked at 123 million tons in 1997. In that same period China's rice production dropped 4 percent. The world's most populous nation may soon be importing massive quantities of grain.

But water shortages are even more worrying in India. There the margin between food consumption and survival is more precarious. Millions of irrigation wells have dropped water tables in almost every state. As Fred Pearce reported in *New Scientist:*

> Half of India's traditional hand-dug wells and millions of shallower tube wells have already dried up, bringing a spate of suicides among those who rely on them. Electricity blackouts are reaching epidemic proportions in states where half of the electricity is used to pump water from depths of up to a kilometer [3,300 feet].

A World Bank study reports that 15 percent of India's food supply is produced by mining groundwater. Stated otherwise, 175 million Indians consume grain produced with water from irrigation wells that will soon be exhausted. The continued shrinking of water supplies could lead to unmanageable food shortages and social conflict.

### Less Soil, More Hunger

The scope of the second worrisome trend—the loss of topsoil—is also startling. Topsoil is eroding faster than new soil forms on perhaps a third of the world's cropland. This thin layer of essential plant nutrients, the very foundation of civilization, took long stretches of geologic time to build up, yet it is typically only about six inches deep. Its loss from wind and water erosion doomed earlier civilizations.

In 2002 a U.N. team assessed the food situation in Lesotho, the small, landlocked home of two million people embedded within South Africa. The team's finding was straightforward: "Agriculture in Lesotho faces a catastrophic future; crop production is declining and could cease altogether over large tracts of the country if steps are not taken to reverse soil erosion, degradation and the decline in soil fertility."

In the Western Hemisphere, Haiti—one of the first states to be recognized as failing—was

KOREAN FEDERATION FOR ENVIRONMENTAL MOVEMENT *(Brown)*; SAMUEL VELASCO 5W Infographics *(illustration)* largely self-sufficient in grain 40 years ago. In the years since, though, it has lost nearly all its forests and much of its topsoil, forcing the country to import more than half of its grain.

The third and perhaps most pervasive environmental threat to food security—rising surface temperature—can affect crop yields everywhere. In many countries crops are grown at or near their thermal optimum, so even a minor temperature rise during the growing season can shrink the harvest. A study published by the U.S. National Academy of Sciences has confirmed a rule of thumb among crop ecologists: for every rise of one degree Celsius (1.8 degrees Fahrenheit) above the norm, wheat, rice and corn yields fall by 10 percent.

In the past, most famously when the innovations in the use of fertilizer, irrigation and high-yield varieties of wheat and rice created the "green revolution" of the 1960s and 1970s, the response to the growing demand for food was the successful application of scientific agriculture: the technological fix. This time, regrettably, many of the most productive advances in agricultural technology have already been put into practice, and so the long-term rise in land productivity is slowing down. Between 1950 and 1990 the world's farmers increased the grain yield per acre by more than 2 percent a year, exceeding the growth of population. But since then, the annual growth in yield has slowed to slightly more than 1 percent. In some countries the yields appear to be near their practical limits, including rice yields in Japan and China.

Some commentators point to genetically modified crop strains as a way out of our predicament. Unfortunately, however, no genetically modified crops have led to dramatically higher yields, comparable to the doubling or tripling of wheat and rice yields that took place during the green revolution. Nor do they seem likely to do so, simply because conventional plant-breeding techniques have already tapped most of the potential for raising crop yields.

## Jockeying for Food

As the world's food security unravels, a dangerous politics of food scarcity is coming into play: individual countries acting in their narrowly defined self-interest are actually worsening the plight of the many. The trend began in 2007, when leading wheat-exporting countries such as Russia and Argentina limited or banned their exports, in hopes of increasing locally available food supplies and thereby bringing down food prices domestically. Vietnam, the world's second-biggest rice exporter after Thailand, banned its exports for several months for the same reason. Such moves may reassure those living in the exporting countries, but they are creating panic in importing countries that must rely on what is then left of the world's exportable grain.

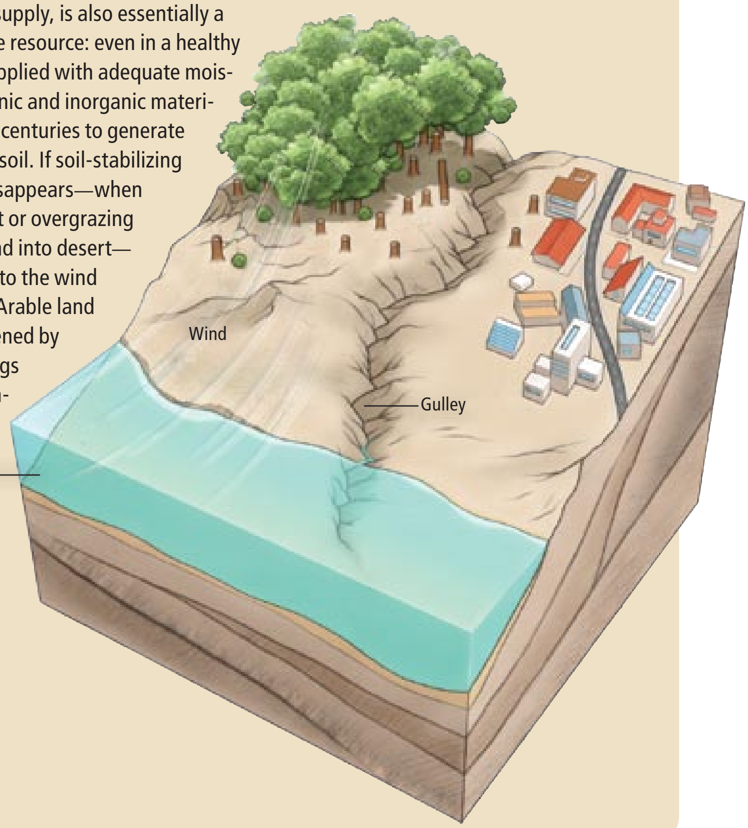
In response to those restrictions, grain importers are trying to nail down long-term bilateral trade agreements that would lock up future grain supplies. The Philippines, no longer able to count on getting rice from the world market, recently negotiated a three-year deal with Vietnam for a guaranteed 1.5 million tons of rice each year. Food-import anxiety is even spawning entirely new efforts by food-importing countries to buy or lease farmland in other countries [*see sidebar at top of next page*].

In spite of such stopgap measures, soaring food prices and spreading hunger in many other countries are beginning to break down the social order. In several provinces of Thailand the predations of "rice rustlers" have forced villag-

[ERODING SOILS]

### Arable Land Is Disappearing

Topsoil, another vital factor in maintaining the world's food supply, is also essentially a nonrenewable resource: even in a healthy ecosystem supplied with adequate moisture and organic and inorganic material, it can take centuries to generate an inch of topsoil. If soil-stabilizing vegetation disappears—when forests are cut or overgrazing turns grassland into desert—topsoil is lost to the wind and the rain. Arable land is also threatened by roads, buildings and other nonfarm usage.




### HOW FAILED STATES THREATEN EVERYONE

**When a nation's government can no longer provide security or basic services for its citizens, the resulting social chaos can have serious adverse effects beyond that nation's own borders:**

- **Spreading disease**
- **Offering sanctuary to terrorists and pirates**
- **Spreading the sale of drugs and weapons**
- **Fostering political extremism**
- **Generating violence and refugees, which can spill into neighboring states**

SAMUEL VELASCO 5W Infographics

## SIDE BETS IN THE GAME OF FOOD POLITICS

**Anxious to ensure future grain supplies, several nations are quietly making deals with grain-producing countries for rights to farm there. The practice tightens supplies for other importing nations and raises prices. Some examples:**

- **China:** Seeking to lease land in **Australia, Brazil, Burma (Myanmar), Russia** and **Uganda**
- **Saudi Arabia:** Looking for farmland in **Egypt, Pakistan, South Africa, Sudan, Thailand, Turkey** and **Ukraine**
- **India:** Agribusiness firms pursuing cropland in **Paraguay** and **Uruguay**
- **Libya:** Leasing 250,000 acres in **Ukraine** in exchange for access to Libyan oil fields
- **South Korea:** Seeking land deals in **Madagascar, Russia** and **Sudan**

ers to guard their rice fields at night with loaded shotguns. In Pakistan an armed soldier escorts each grain truck. During the first half of 2008, 83 trucks carrying grain in Sudan were hijacked before reaching the Darfur relief camps.

No country is immune to the effects of tightening food supplies, not even the U.S., the world's breadbasket. If China turns to the world market for massive quantities of grain, as it has recently done for soybeans, it will have to buy from the U.S. For U.S. consumers, that would mean competing for the U.S. grain harvest with 1.3 billion Chinese consumers with fast-rising incomes—a nightmare scenario. In such circumstances, it would be tempting for the U.S. to restrict exports, as it did, for instance, with grain and soybeans in the 1970s when domestic prices soared. But that is not an option with China. Chinese investors now hold well over a trillion U.S. dollars, and they have often been the leading international buyers of U.S. Treasury securities issued to finance the fiscal deficit. Like it or not, U.S. consumers will share their grain with Chinese consumers, no matter how high food prices rise.

### Plan B: Our Only Option

Since the current world food shortage is trend-driven, the environmental trends that cause it must be reversed. To do so requires extraordinarily demanding measures, a monumental shift away from business as usual—what we at the Earth Policy Institute call Plan A—to a civilization-saving Plan B.

Similar in scale and urgency to the U.S. mobilization for World War II, Plan B has four components: a massive effort to cut carbon emissions by 80 percent from their 2006 levels by 2020; the stabilization of the world's population at eight billion by 2040; the eradication of poverty; and the restoration of forests, soils and aquifers.

Net carbon dioxide emissions can be cut by systematically raising energy efficiency and investing massively in the development of renewable sources of energy. We must also ban deforestation worldwide, as several countries already have done, and plant billions of trees to sequester carbon. The transition from fossil fuels to renewable forms of energy can be driven by imposing a tax on carbon, while offsetting it with a reduction in income taxes.

Stabilizing population and eradicating poverty go hand in hand. In fact, the key to accelerating the shift to smaller families is eradicating poverty—and vice versa. One way is to ensure at least a primary school education for all children, girls as well as boys. Another is to provide rudimentary, village-level health care, so that people can be confident that their children will survive to adulthood. Women everywhere need access to reproductive health care and family-planning services.

The fourth component, restoring the earth's natural systems and resources, incorporates a worldwide initiative to arrest the fall in water tables by raising water productivity: the useful activity that can be wrung from each drop. That implies shifting to more efficient irrigation systems and to more water-efficient crops. In some countries, it implies growing (and eating) more wheat and less rice, a water-intensive crop. And for industries and cities, it implies doing what some are doing already, namely, continuously recycling water.

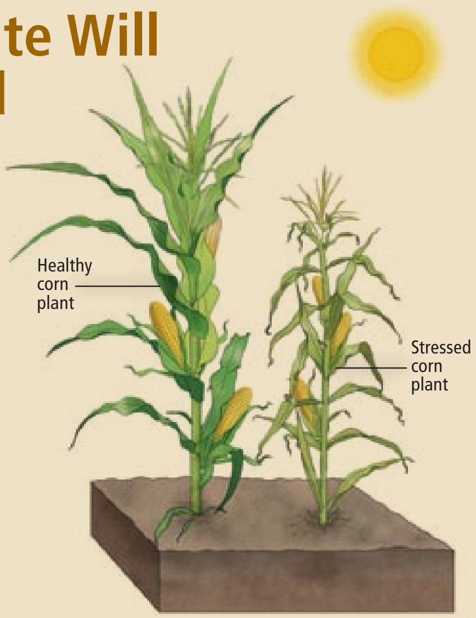
At the same time, we must launch a worldwide effort to conserve soil, similar to the U.S. response to the Dust Bowl of the 1930s. Terracing the ground, planting trees as shelterbelts against windblown soil erosion, and practicing minimum tillage—in which the soil is not plowed and crop residues are left on the field—are among the most important soil-conservation measures.

There is nothing new about our four interrelated objectives. They have been discussed individually for years. Indeed, we have created entire institutions intended to tackle some of them, such as the World Bank to alleviate poverty.

[RISING TEMPERATURES]

### Hotter Climate Will Reduce Yield

Agriculture as it exists today has been shaped by a climate system that has changed little in the 11,000-year history of farming. Because most crops were developed for maximum production under these stable conditions, the higher temperatures that are expected from global warming will reduce crop yield, measured in bushels per acre harvested. Crop ecologists reckon that for every rise of one degree Celsius (1.8 degrees Fahrenheit) above the norm, wheat, rice and corn yields fall by 10 percent.



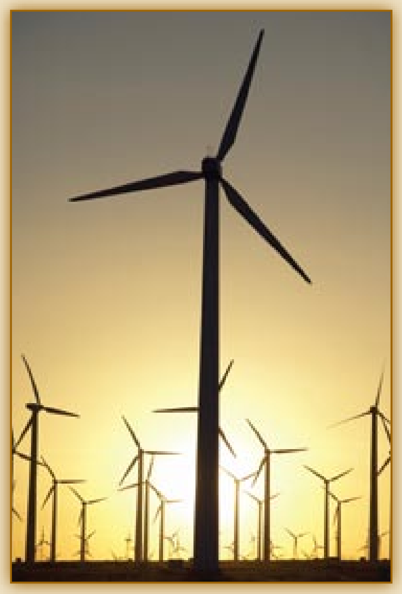

SAMUEL VELASCO *5W Infographics*

[SOLUTIONS]

# WHAT IS TO BE DONE?

Plan B, the author's road map to correcting the factors that threaten our civilization, has four main components: a massive effort to cut carbon emissions by 80 percent from their 2006 levels by 2020; the stabilization of the world's population at eight billion or fewer by 2040; the eradication of poverty; and the restoration of the planet's forests, soils and aquifers. This box highlights a few of the major actions needed to accomplish these goals.



▲ Replace fossil fuels with renewables for electricity and heat.

▲ Offer universal basic health care, reproductive health care and family planning.

◀ Plant trees to reduce flooding, conserve soil, sequester carbon and halt net deforestation.


▲ Recycle wastewater to raise its productivity, as this sewage treatment plant does for Orange County, California.

SONNY TUMBELAKA *Getty Images (planting tree)*; GETTY IMAGES *(windmills)*; ANDREW CABALLERO-REYNOLDS *Getty Images (immunization)*; MARY KNOX MERRILL *Getty Images (treatment plant)*

And we have made substantial progress in some parts of the world on at least one of them—the distribution of family-planning services and the associated shift to smaller families that brings population stability.

For many in the development community, the four objectives of Plan B were seen as positive, promoting development as long as they did not cost too much. Others saw them as humanitarian goals—politically correct and morally appropriate. Now a third and far more momentous rationale presents itself: meeting these goals may be necessary to prevent the collapse of our civilization. Yet the cost we project for saving civilization would amount to less than $200 billion a year, a sixth of current global military spending. In effect, Plan B is the new security budget.

## Time: Our Scarcest Resource

Our challenge is not only to implement Plan B but also to do it quickly. The world is in a race between political tipping points and natural ones. Can we close coal-fired power plants fast enough to prevent the Greenland ice sheet from slipping into the sea and inundating our coastlines? Can we cut carbon emissions fast enough to save the mountain glaciers of Asia? During the dry season their meltwaters sustain the major rivers of India and China—and by extension, hundreds of millions of people. Can we stabilize population before countries such as India, Pakistan and Yemen are overwhelmed by shortages of the water they need to irrigate their crops?

It is hard to overstate the urgency of our predicament. Every day counts. Unfortunately, we do not know how long we can light our cities with coal, for instance, before Greenland's ice sheet can no longer be saved. Nature sets the deadlines; nature is the timekeeper. But we human beings cannot see the clock.

We desperately need a new way of thinking, a new mind-set. The thinking that got us into this bind will not get us out. When Elizabeth Kolbert, a writer for the *New Yorker*, asked energy guru Amory Lovins about thinking outside the box, Lovins responded: "There is no box."

There is no box. That is the mind-set we need if civilization is to survive. ■

## ➥ MORE TO EXPLORE

**Outgrowing the Earth: The Food Security Challenge in an Age of Falling Water Tables and Rising Temperatures.** Lester R. Brown. W. W. Norton, Earth Policy Institute, 2004. Available at **www.earthpolicy.org/Books/Out/Contents.htm**

**Collapse: How Societies Choose to Fail or Succeed.** Jared Diamond. Penguin, 2005.

**Climate Change 2007.** Fourth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, 2007. Available at **www.ipcc.ch**

**Plan B 3.0: Mobilizing to Save Civilization.** Lester R. Brown. W. W. Norton, Earth Policy Institute, 2008. Available at **www.earthpolicy.org/Books/PB3**


# How to Steal Secrets

## Information thieves can now do an end run around encryption, networks and the operating system > > > BY W. WAYT GIBBS

Through the eyepiece of Michael Backes's small Celestron telescope, the 18-point letters on the laptop screen at the end of the hall look nearly as clear as if the notebook computer were on my lap. I do a double take. Not only is the laptop 10 meters (33 feet) down the corridor, it faces away from the telescope. The image that seems so legible is a reflection off a glass teapot on a nearby table. In experiments here at his laboratory at Saarland University in Germany, Backes has discovered that an alarmingly wide range of objects can bounce secrets right off our screens and into an eavesdropper's camera. Spectacles work just fine, as do coffee cups, plastic bottles, metal jewelry—even, in his most recent work, the eyeballs of the computer user. The mere act of viewing information can give it away.

The reflection of screen images is only one of the many ways in which our computers may leak information through so-called side channels, security holes that bypass the normal encryption and operating-system restrictions we rely on to protect sensitive data. Researchers recently demonstrated five different ways to surreptitiously capture keystrokes, for example, without installing any software on the target computer. Technically sophisticated observers can extract private data by reading the flashing light-emitting diodes (LEDs) on network switches or by scrutinizing the faint radio-frequency waves that every monitor emits. Even certain printers make enough noise to allow for acoustic eavesdropping.

Outside of a few classified military programs, side-channel attacks have been largely ignored by computer security researchers, who

JEN CHRISTIANSEN (*photoillustration of reflection*); DIGITAL VISION/GETTY IMAGES (*man with glasses*)

# without a Network

have instead focused on creating ever more robust encryption schemes and network protocols. Yet that approach can secure only information that is inside the computer or network. Side-channel attacks exploit the unprotected area where the computer meets the real world: near the keyboard, monitor or printer, at a stage before the information is encrypted or after it has been translated into human-readable form. Such attacks also leave no anomalous log entries or corrupted files to signal that a theft has occurred, no traces that would allow security researchers to piece together how frequently they happen. The experts are sure of only one thing: whenever information is vulnerable and has significant monetary or intelligence value, it is only a matter of time until someone tries to steal it.

## From Tempest to Teapot

The idea of stealing information through side channels is far older than the personal computer. In World War I the intelligence corps of the warring nations were able to eavesdrop on one another's battle orders because field telephones of the day had just one wire and used the earth to carry the return current. Spies connected rods in the ground to amplifiers and picked up the conversations. In the 1960s American military scientists began studying the radio waves given off by computer monitors and launched a program, code-named "Tempest," to develop shielding techniques that are used to this day in sensitive government and banking computer systems. Without Tempest shielding, the image being scanned line by line onto the screen of a standard cathode-ray tube monitor can be reconstructed from a nearby room—or even an adjacent building—by tuning into the monitor's radio transmissions.

Many people assumed that the growing popularity of flat-panel displays would make Tempest problems obsolete, because flat panels use low voltages and do not scan images one line at a time. But in 2003 Markus G. Kuhn, a computer scientist at the University of Cambridge Computer Laboratory, demonstrated that even flat-

### KEY CONCEPTS

- Even with the best network security, your electronic data may not be safe from a determined hacker.
- Researchers have extracted information from nothing more than the reflection of a computer monitor off an eyeball or the sounds emanating from a printer.
- These attacks are difficult to defend against and impossible to trace.

*—The Editors*

# Anatomy of a Vulnerable Office

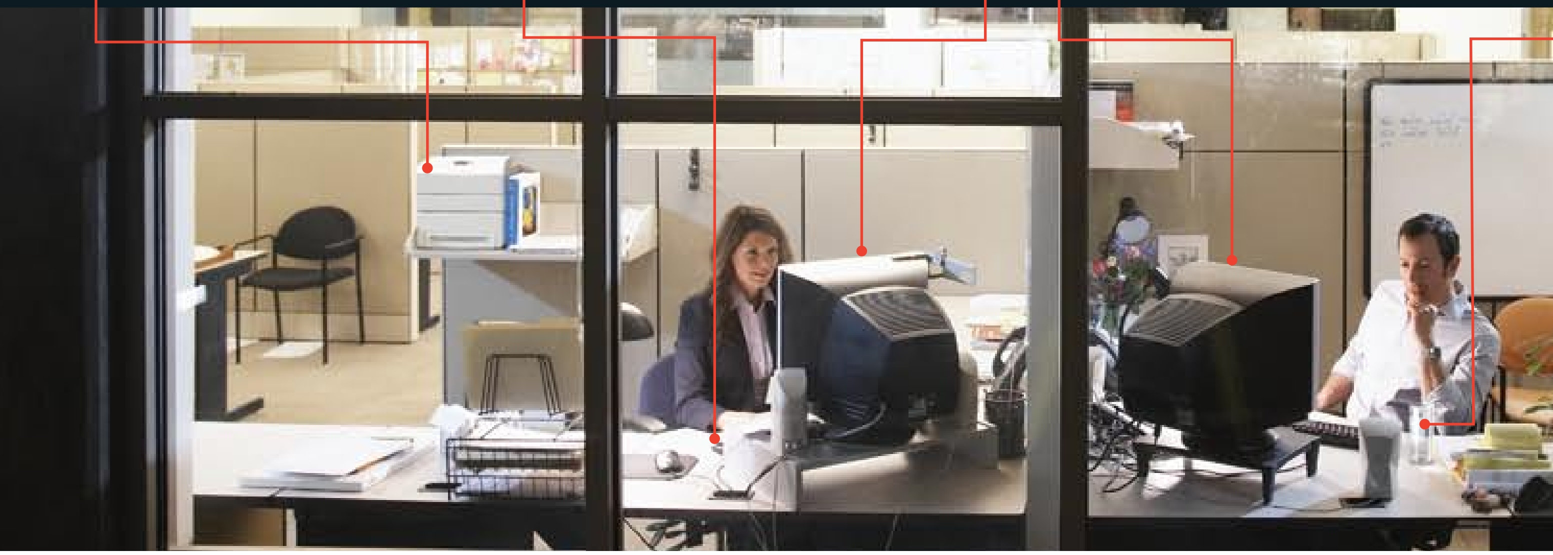
Researchers have figured out how to turn your office against you. Every reflection, every sound, every invisible pulse of electromagnetic radiation has the potential to reveal secret data to a trained eye. Here are a few of the vulnerabilities that have been exposed by academic experts. As for the less forthcoming experts, we can only guess what they have found.

**WEBCAM** Click on the wrong link in an e-mail or a Web page, and a spy can take over any camera attached to your computer. By joining Webcam data with a new automated system called ClearShot that deciphers keystrokes through video, an eavesdropper could record everything you type.

**PRINTER** A dot-matrix printer creates sounds that can later be used to reconstruct the individual words that were being printed [*see box on opposite page*]. One group is now attempting to extend the trick to the far more ubiquitous ink-jet printer.

**KEYBOARD** Each key emits a unique radio-wave signature when it is pressed. Two graduate students recently demonstrated that, based on those waves, they could reconstruct a person's keystrokes using a simple wire antenna located 20 meters away and separated by a wall.

**COMPUTER MONITOR** Researchers once thought that only old-fashioned cathode-ray tube monitors (such as the ones pictured here) emit enough electromagnetic radiation for a spy to reconstruct the image on a screen. But new research shows that even flat-screen LCD monitors are vulnerable.



JEN CHRISTIANSEN (*photoillustration of printer and cup*); THOMAS NORTHCUT *Digital Vision* (*office scene*)

panel monitors, including those built into laptops, radiate digital signals from their video cables, emissions that can be picked up and decoded from many meters away. The monitor refreshes its image 60 times or more each second; averaging out the common parts of the pattern leaves just the changing pixels—and a readable copy of whatever the target display is showing.

"Thirty years ago only military suppliers had the equipment necessary to do the electromagnetic analysis involved in this attack," Kuhn says. "Today you can find it in any well-equipped electronics lab, although it is still bulky. Sooner or later, however, it will be available as a plug-in card for your laptop."

Similarly, commonplace radio surveillance equipment can pick up keystrokes as they are typed on a keyboard in a different room, according to Martin Vuagnoux and Sylvain Pasini, both graduate students in computer science at the Swiss Federal Institute of Technology in Lausanne. The attack does not depend on fluctuations in the power supply, so it works even on the battery-powered laptops you see by the dozen in any airport terminal.

Vuagnoux and Pasini showed off the feat in an online video recorded last October. They are now preparing a conference paper that describes four distinct ways that keystrokes can be deduced from radio signals captured through walls at distances up to 20 meters. One of the newer methods is 95 percent accurate. "The way the keyboard determines which key is pressed is by polling a matrix of row and column lines," explains Kuhn, who proposed (but never demonstrated) one of these methods a decade ago. "The polling process emits faint radio pulses, and the position of those pulses in time can reveal which key was pressed."

Last May a group led by Giovanni Vigna of the University of California, Santa Barbara, published details of a fifth way to capture typing that does not require a fancy radio receiver; an ordinary webcam and some clever software will do. Vigna's software, called ClearShot, works on video of a victim's fingers typing on a keyboard. The program combines motion-tracking algorithms with sophisticated linguistic models to deduce the most probable words being typed. Vigna reports that ClearShot re-

**GLASS REFLECTIONS** Curved glass is perfect for snooping, because it captures reflections from a wide area of the room. With computer-based techniques for correcting the image [*see box on next page*], a spy could record images of your computer screen.

**WHITEBOARD** Images can also be pulled off any other reflective surface—a wall clock, a metal coffee carafe or a whiteboard.

constructs the typed text about as quickly as human volunteers do, but not quite as accurately.

It might seem implausible that someone would allow their own webcam to be used against them in this way. It is not. Gathering video from a webcam can be as simple as tricking the user into clicking on an innocuous-looking link in a Web page, a process known as clickjacking. Last October, Jeremiah Grossman of WhiteHat Security and Robert Hansen of SecTheory revealed details of bugs they discovered in many Web browsers and in Adobe's Flash software that together allow a hostile Web site to collect audio and video from a computer's microphone and webcam. Just a single errant click launches the surveillance.

## Eye See You

Still, Backes points out, "almost all these interception methods are accessible only to experts with specialized knowledge and equipment. What distinguishes the attack based on reflections is that almost anyone with a $500 telescope can do it, and it is almost impossible to defend against completely."

Backes, a fellow of the Max Planck Institute for Software Systems in Saarbrücken, Germany, who made a name for himself at IBM's research lab in Zurich before entering academia, spends most of his time working on the mathematics that underlies cryptography. But every year he works on a new project with his students just for fun. This year they wrote computer code that translates an audio recording of a dot-matrix printer—the noisy variety that is still often used by airlines, banks and hospitals—into a picture of the page that was being printed at the time. Based on the success of that work, Backes's group has been performing experiments to determine whether the method could be extended to retrieve text from recordings of ink-jet printers. "Obviously, this is much harder because ink-jets are so quiet," Backes says.

Last year the idea for the annual fun project dawned on Backes as he was walking past the office where his graduate students were furious-

**Side-channel leaks offer the easiest way to bypass elaborate network security systems—and they do it without leaving a trail.**

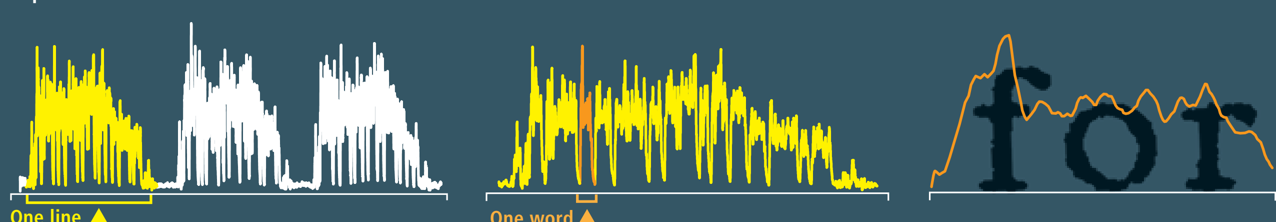
[AUDIO SURVEILLANCE]

## HOW TO SPY ON A PRINTER

Inside a dot-matrix printer, a printhead scans a number of tiny pins back and forth against an ink ribbon. Each letter creates a unique sound—for example, tall letters require more pins and thus make a louder noise. Yet the correlation is not perfect, and so researchers put the initial guess of what the printed message is through an additional linguistic analysis that determines the most reasonable letter sequence.

**FROM AUDIO TO LETTER FORMS**

**A plot of volume across time for three lines → A closer look at one line → And one word**



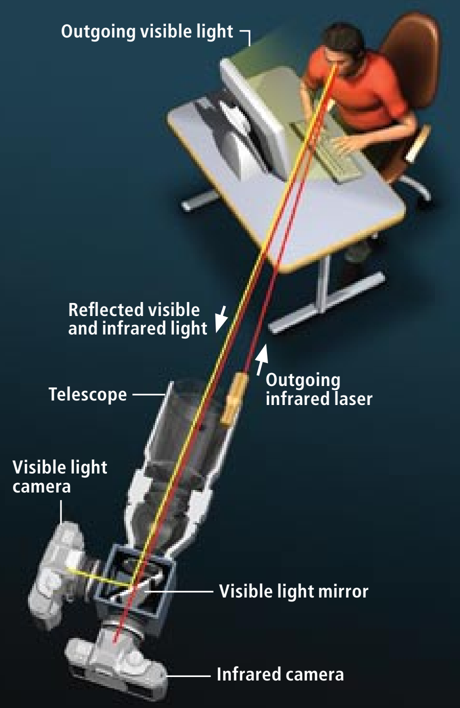

JEN CHRISTIANSEN; SOURCE: MARKUS DUERMUTH

[VIDEO SURVEILLANCE]

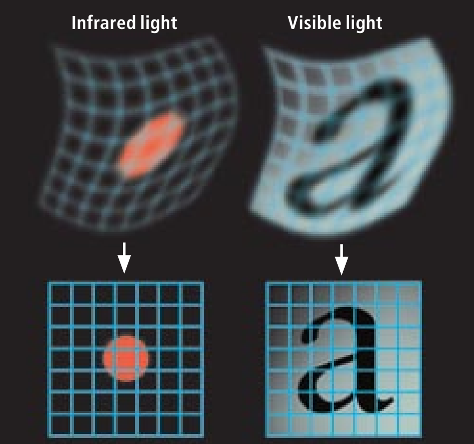
# HOW TO READ AN EYEBALL

Although your eyeball reflects your monitor, any potential spy would have to overcome substantial obstacles to record a usable image of the screen contents. Any powerful telescope directed at you will have a wide aperture and thus could bring into focus only a very narrow slice of the world—anything a few millimeters in front of or behind the focus point will appear blurry. In addition, the constant motion of our eyes blurs any exposure lasting over a few hundredths of a second. To correct these problems, the spy could use an adaptive optics system (*diagram*). The system would bounce a laser beam (infrared so as not to be noticed) off the eyeball, then record what the reflected beam looks like in a camera separate from the one that captures the visible image.

## SETUP




## DECONVOLUTION




▲ The spy would then run the image of the laser beam through a deconvolution process. The reflection of the beam appears smudged, yet the spy knows that the laser beam was originally a perfect circle. A computer program determines how to best manipulate the smudge to return it to its original state, then performs these same operations on the blurry photograph containing the stolen information. End result: the blurry image comes into focus.

ly typing away. "'What are they working on so hard?' I wondered," Backes says. As he noticed a small blue-white patch in a teapot on one student's desk and realized it was the reflection of the computer screen, the idea struck. "The next day I went to a hobby shop and bought an ordinary backyard telescope [for $435] and a six-megapixel digital camera."

The setup worked surprisingly well. Medium-size type was clearly legible when the telescope was aimed at reflections in a spoon, a wine glass, a wall clock. Nearly any shiny surface worked, but curved surfaces worked best, because they revealed wide swathes of the room, thus eliminating the need for a peeping hacker to find a sweet spot where the reflected screen is visible. Unfortunately, all of us who use computer screens have nearly spherical, highly reflective objects stuck to our faces. Could digital secrets be read off the eyes of their beholders?

Backes knew he would need a bigger telescope and a more sensitive camera to find out. Because eyeballs are rarely still for more than a second or so, the shutter speed on the camera would have to be fast to reduce motion blur. "For eyes, it is the brightness of the reflected image, not its resolution, that limits how far away a spy can be," Backes says.

He bought a $1,500 telescope and borrowed a $6,000 astronomical camera from the Max Planck Institute for Astronomy in Heidelberg, Germany. Now he was able to make out 72-

**SIZE VS. DISTANCE: A spy attempting to read a reflection is limited by the aperture (or width) of his telescope. A telescope that is too narrow will diffract the light coming into it, thus obscuring text. Yet larger telescopes are not only more expensive, they are also more difficult to conceal. The diagram below indicates the telescope size a spy would need at a given distance if the aim were to read 14-point type reflected in an 85-millimeter-wide coffee mug. To read features in an eye, the spy would have to be much closer—divide these distances by about a factor of four.**


DON FOLEY (*setup*); LUCY READING-IKKANDA (*telescope lineup*); JEN CHRISTIANSEN (*diagram*) point text in the eye of a target 10 meters away.

He figured he could do even better by borrowing something else from astronomy: a process called deconvolution that removes blur in photographs of distant galaxies. The idea is to measure how a point of light in the original image (such as a star or a reflected status LED on a monitor) smears when captured by the camera. A mathematical function can then reverse the blurring to restore the point, sharpening the rest of the image at the same time [*see box on opposite page*]. The deconvolution software lowered the threshold of legibility to 36-point type at 10 meters for a telescope that could easily be hidden inside a car. A van-size telescope could do even better.

Backes will present his results this month at the IEEE Symposium on Security and Privacy, but he already has ideas for further improvement. "A real attacker could train an invisible laser on the target," he notes. That would enable autofocusing on the eyeball and better deconvolution of the motion blur. Spies could take advantage of software from HeliconSoft that can assemble one clear image of an object by combining many partially blurry images; only those regions that are in focus are retained. They could also exploit software for high dynamic-range imaging that uses similar techniques to create one high-contrast photograph from images shot with a variety of exposures.

## A Blind Defense

Protecting ourselves against our overly communicative computers is much harder in some ways than defending against spam, phishing and viruses. There is no convenient software package one can install to dam the side channels. On the other hand, it is not clear that anyone is actively exploiting them. Backes and Kuhn say it is safe to assume that military organizations have used the techniques to gather intelligence, but they can cite no specific examples.

The blinds in Backes's office were drawn as we discussed these possibilities, and curtains are one obvious way of frustrating a reflection thief. But Backes points out that it is naive to expect that people will always remember, or be able, to cover their windows. Although many laptop users apply "privacy filters" to their screens to protect against over-the-shoulder eavesdropping, these filters increase the brightness of the reflection on the viewer's eyes, thus making the hacker's job easier.

Flat-panel displays emit polarized light, so a polarizing film on a window could in principle block reflections from every screen in the room. In practice, however, this fix does not work. Small variations in the polarization angle of displays are common, and the resulting small mismatches let enough light escape that a good telescope can still make out the screen.

Compared with conventional forms of computer espionage, side-channel attacks do have a couple of major limitations, Kuhn notes. "You have to be close to the target, and you must be observing while a user is actively accessing the information. It's much easier if you can instead convince someone to open an e-mail attachment and install malicious software that opens a back door to their entire system. You can do that to millions of people at once."

For that reason, side-channel hacks are unlikely to become as common as spam, malware and other assaults through the network. Instead they will likely be used to infiltrate a few highly lucrative targets, such as the computers of financiers and high-level corporate and government officials. In these cases, side-channel leaks probably offer the easiest way to bypass elaborate network security systems and do it without leaving any trail that a security team could trace after the fact. Anecdotal evidence suggests such surveillance is already taking place. "Some people in investment banks cite cases where information has disappeared, and they are certain it wasn't a traditional attack such as a software hack or the cleaning lady duplicating a hard disk," Kuhn says. "But to my knowledge, no one has ever been caught in the act." ■

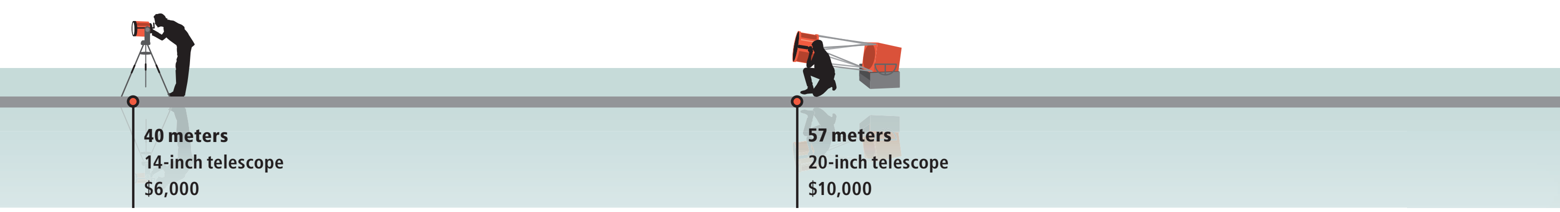
*W. Wayt Gibbs, a contributing editor at* Scientific American, *is executive editor at Intellectual Ventures in Bellevue, Wash.*

## ➥ MORE TO EXPLORE

**ClearShot: Eavesdropping on Keyboard Input from Video.** Davide Balzarotti, Marco Cova and Giovanni Vigna in *Proceedings of the IEEE Symposium on Security and Privacy,* pages 170–183; May 18–22, 2008.

**Compromising Reflections, or, How to Read LCD Monitors around the Corner.** Michael Backes, Markus Dürmuth and Dominique Unruh in *Proceedings of the IEEE Symposium on Security and Privacy,* pages 158–169; May 18–22, 2008.

**Compromising Electromagnetic Emanations of Wired and Wireless Keyboards.** Martin Vuagnoux and Sylvain Pasini. Swiss Federal Institute of Technology Web site: **http://lasecwww.epfl.ch/keyboard**



# PROGRESS IN TISSUE ENGINEERING

By Ali Khademhosseini, Joseph P. Vacanti and Robert Langer

## Pioneers in building living tissue report important advances over the past decade

**KEY CONCEPTS**

- Efforts to build living tissue replacements have progressed over the past decade, and some simple engineered tissues are already used in humans.
- Advances have come from a greater understanding of cell behavior and sophisticated new building materials.
- More tissue-engineered products are close to commercial readiness but must undergo the complex regulatory scrutiny given to living materials.

*—The Editors*

When two of us (Langer and Vacanti) last wrote in this magazine 10 years ago about prospects for tissue engineering, the very idea that living flesh could be "constructed" by following engineering principles and combining nonliving materials with cells sounded fantastical to many. Yet the need for such transplantable human tissues to replace, restore or enhance organ function was, and remains, urgent. Today nearly 50 million people in the U.S. are alive because of various forms of artificial organ therapy, and one in every five people older than 65 in developed nations is very likely to benefit from organ replacement technology during the remainder of their lives.

Current technologies for organ substitution, such as whole-organ transplants and kidney dialysis machines, have saved many lives, but they are imperfect solutions that come with heavy burdens for patients. Engineered biological tissues are customizable and immune-compatible and can therefore potentially make a significant difference in the lives of people with failing organs. They can fill other human needs as well, for example, serving as "organs on a chip" for testing the toxicity of candidate drugs.

Engineered tissues can take many forms, from aggregations or thin sheets of cells to thick constructs of complex tissue and, the ultimate engineering challenge, an entire functioning organ. Since we initially presented the obstacles involved in creating these implantable tissues [see "Tissue Engineering: The Challenges Ahead," by Robert S. Langer and Joseph P. Vacanti; Scientific American, April 1999], scientists have made considerable progress. Products such as skin substitutes and cartilage replacements have already helped thousands of patients. Artificial tissues such as bladder, cornea, bronchial tubes and blood vessels are in clinical trials. And laboratory work on building more complex tissue structures is producing encouraging results.

Although some of the obstacles we described 10 years ago remain, significant advances over the past decade have come from new insights into the way the body naturally builds tissues, during both embryonic development and natural wound healing. And engineering approaches to assembling tissue structures have become more sophisticated, as have the chemical, biological and mechanical properties of the materials available for the task. As a result, the field is coming of age, and tissue-engineered products are increasingly a realistic option for medical treatment.

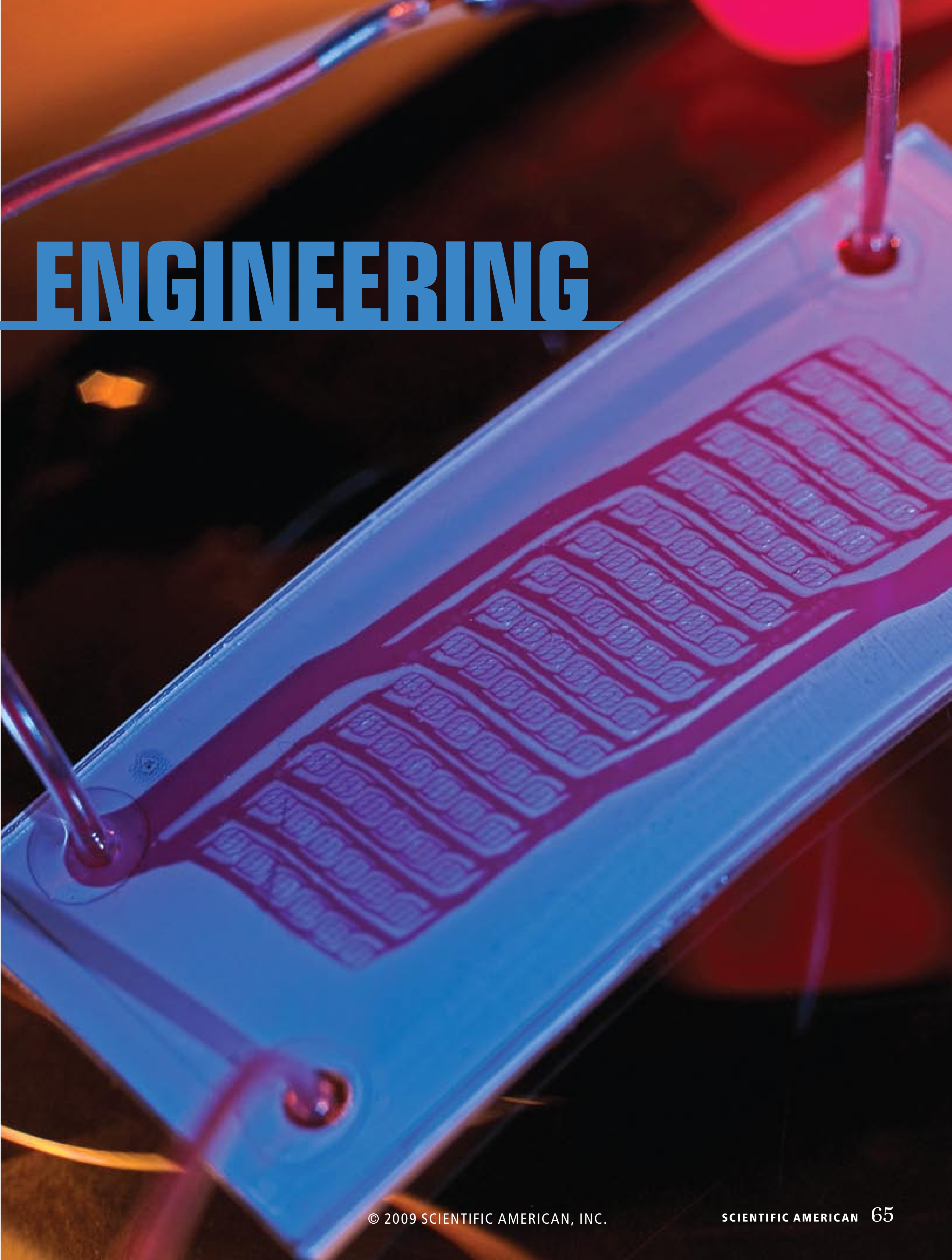
### Delivering Life's Blood

One reason that tissues such as skin and cartilage were among the first to be ready for human testing is that they do not require extensive internal vasculature. But most tissues do, and

**TISSUE CULTURE DEVICE containing microfabricated "blood vessels" is one of the advances made possible by novel materials and technologies available to tissue engineers. A membrane containing nanoscale pores separates the artificial vessels from a layer of liver cells.**

"MICROFABRICATION OF THREE-DIMENSIONAL ENGINEERED SCAFFOLDS," BY JEFFREY T. BORENSTEIN, ELI J. WEINBERG, BRIAN K. ORRICK, CATHRYN SUNDBACK, MOHAMMAD R. KAAZEMPUR-MOFRAD AND JOSEPH P. VACANTI, IN *TISSUE ENGINEERING*, VOL. 13, NO. 8; 2007

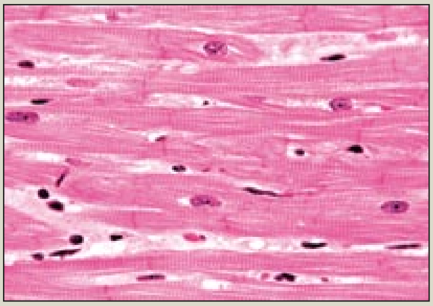
# ENGINEERING



[THE GOAL]

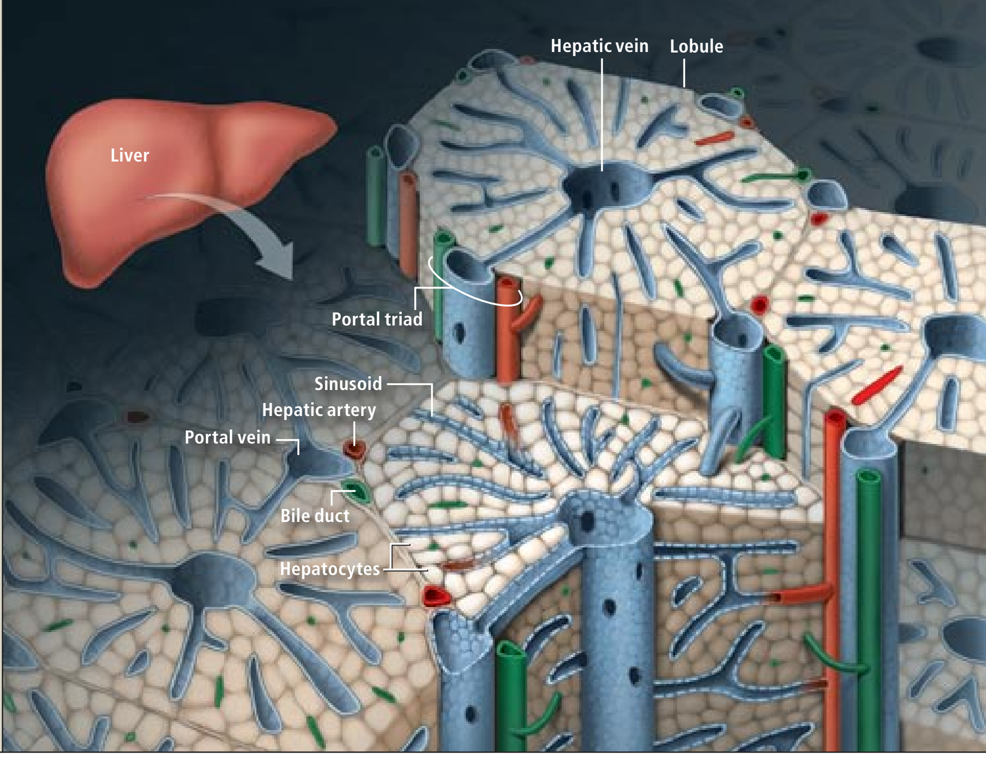
# COPYING NATURE'S ARCHITECTURE

The health and functioning of a natural tissue depend closely on its internal structure. Tissues are made up of multiple cell types that work together to accomplish an organ's task—in the case of the liver (*right*), that is mainly to act as a giant blood filter, whereas heart tissue (*below*) forms a muscular pump. Because cues exchanged between cells and their surroundings are critical to a tissue's development and maintenance as well as its work, the engineer's challenge in building a replacement tissue is to mimic the organ's complex natural organization using a mixture of engineered materials and living cells.



▲ The heart is made up of long fibrous muscle cells, wrapped in collagen sheaths and interwoven with blood vessels. Collagen also connects the muscle bundles end to end and conducts the neural signals that control their contractions. The shape and orientation of muscle cells within heart tissue are therefore critical to their electrical and mechanical properties.

▼ A human liver is organized into roughly hexagonal columns called lobules, each containing spongy tissue radiating around a central hepatic vein. At the corners of each lobule are the so-called portal triads consisting of the hepatic artery, bile duct and portal vein. Blood from both the hepatic vein and hepatic artery percolates through the lobule's rows of cells (*hepatocytes*), which are interleaved with endothelial cells that form broad capillaries known as sinusoids. The liver's repeating lobule structure maximizes blood delivery to the hepatocytes, which extract and break down nutrients and toxins.




the difficulty of providing a blood supply has always limited the size of engineered tissues. Consequently, many scientists are focusing on designing blood vessels and incorporating them in engineered tissues.

Any tissue that is more than a few 100 microns thick needs a vascular system because every cell in a tissue needs to be close enough to capillaries to absorb the oxygen and nutrients that diffuse constantly out of those tiny vessels. When deprived of these fuels, cells quickly become irreparably damaged.

In the past few years a number of new approaches to building blood vessels—both outside tissues and within them—have been devised. Many techniques rely on an improved understanding of the environmental needs of endothelial cells (which form capillaries and line larger vessels), as well as an advanced ability to sculpt materials at extremely small scales. For example, when endothelial cells are laid on a bed of scaffolding material whose surface is patterned with nanoscale grooves—1,000th the diameter of a human hair—they are encouraged to form a network of capillarylike tubes [*see box on page 69*]. The grooves mimic the texture of body tissues that endothelial cells rest against while forming natural blood vessels, thus providing an important environmental signal.

**The difficulty of providing a blood supply has always limited the size of engineered tissues.**

Microfabrication, the set of techniques used to etch microelectronics chips for computers and mobile phones, has also been employed to make capillary networks. Vacanti, with Jeffrey T. Borenstein of the Draper Laboratory in Cambridge, Mass., has generated arrays of microchannels to mimic tissue capillary networks directly within degradable polymer scaffolds, for instance. Inside these channels, endothelial cells can be cultured to form blood vessels while also acting as a natural barrier that minimizes the fouling effect of blood on the scaffold materials. An alternative is to use a membrane filter to separate the blood-carrying channels from the functional cells in a tissue construct [*see illustration on preceding page and box on page 71*].

Another method for keeping cells and blood

INNERSPACE IMAGING *Photo Researchers, Inc.* (*heart muscle cells*); JEN CHRISTIANSEN (*liver diagram*) separate but close enough to exchange a variety of molecules is to suspend them within hydrogels, which are gelatinlike materials made from hydrated networks of polymers. Hydrogels chemically resemble the natural matrix that surrounds all cells within tissues. The functional cells can be encapsulated inside the material, and channels running through the gel can be lined with endothelial cells to engineer tissuelike structures with a protovasculature.

Research from the laboratories of Laura Niklason of Yale University and Langer has shown that larger blood vessels can be generated by exposing scaffolds seeded with smooth muscle cells and endothelial cells to pulsating conditions inside a bioreactor. Arteries made in this environment, which is designed to simulate the flow of blood through vessels in the body, are mechanically robust and remain functional after being transplanted into animals. In addition to enabling tissue engineers to incorporate such vessels into larger constructs, the engineered tubes by themselves may provide grafts for bypass surgery in patients with atherosclerosis.

Although the ability to engineer capillarylike structures and larger blood vessels outside the body is a significant breakthrough, a working engineered tissue implant will have to connect quickly with the recipient's own blood supply if the construct is to survive. Coaxing the body to form new vasculature is therefore an equally important aspect of this work. David Mooney of Harvard University, for example, has demonstrated that the controlled release of chemical growth factors from polymeric beads or from scaffold material itself can promote the formation of blood vessels that penetrate implanted tissue constructs.

Pervasis Therapeutics, with which Langer and Vacanti are affiliated, is conducting advanced clinical trials in which a variation of this principle is applied to healing a vascular injury. A three-dimensional scaffold containing smooth muscle and endothelial cells is transplanted adjacent to the site of the injury to provide growth-stimulating signals and to promote natural rebuilding of the damaged blood vessel [*see bottom photograph at right*].

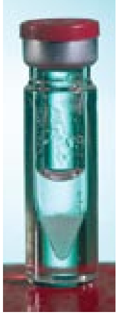
Despite these advances, a number of challenges still remain in making large vascularized tissues and vascular grafts, and scientists have not yet completely solved this problem. New blood vessels grow and penetrate an implanted tissue construct slowly, causing many of the construct's cells to die for lack of a blood supply immediately after implantation. For this reason, tissue-engineering approaches that include a vascular system prefabricated within the tissue construct are very likely to be necessary for large transplants. Such prefabricated vessels may also be combined with controlled release of blood vessel–recruiting growth factors to induce further growth of the construct's vessels.

Because integrating the engineered vasculatures and those of the host is also critical, researchers need a better understanding of the cross talk between the host tissue cells and implanted cells to foster their connection. This need to decipher more of the signals that cells exchange with one another and with their environments also extends to other aspects of building a successful tissue implant, such as selecting the best biological raw materials.

## NO LONGER ON THE HORIZON

**A number of products based on tissue-engineering principles are already being used to treat patients, in clinical trials or as FDA-approved therapies. Examples include simple skin and cartilage, as well as a patch designed to speed tissue healing.**

**SKIN**: Epicel, a permanent replacement epidermis, is grown from the patient's own skin cells and intended to treat burns.



**CARTILAGE**: Carticel, one of the first cell-based treatments to be marketed, is an injectable suspension of cartilage-repairing chondrocytes derived from the patient and cultured with growth-promoting factors.

**VESSEL PATCH**: Vascugel, currently in clinical trials, is a construct made of donor endothelial cells and designed to be placed on top of an injured blood vessel. The healthy patch cells send signals to cells within the damaged vessel that promote healing and reduce inflammation and scarring.

COURTESY OF GENZYME CORPORATION (*Epicel and Carticel*); COURTESY OF JACK HARVEY *Pervasis Therapeutics, Inc.* (*Vascugel*)

## Suitable Cells

In most situations, building an implantable tissue from a patient's own cells would be ideal because they are compatible with that person's immune system. Realistically, such implants might also face fewer regulatory hurdles because the material is derived from the patient's own body. The ability of normal cells to multiply in culture is limited, however, making it difficult to generate sufficient tissue for an implant. So-called adult stem cells from the patient's body or from a donor are somewhat more prolific, and they can be isolated from many sources, including blood, bone, muscle, blood vessels, skin, hair follicles, intestine, brain and liver.

Adult stem cells—which occur in adult tissues and are able to give rise to a variety of cell types characteristic of their native tissue—are difficult to identify, however, because they do not look very different from regular cells. Scientists therefore must look for distinctive surface proteins that serve as molecular markers to flag stem cells. The identification of additional markers would make it considerably easier to work with adult stem cells in tissue-engineering applications. Fortunately, over the past few years a number of major advances have been made, including development of novel methods of isolating the cells and inducing them to proliferate and to differentiate into various tissue types in culture.

Notably, Christopher Chen and Dennis Discher, both at the University of Pennsylvania, have demonstrated that mesenchymal stem cells, which are typically derived from muscle, bone or fat, will respond to mechanical cues from their surroundings. They have been shown to differentiate into the tissue that most closely resembles the stiffness of the substrate material on which they are growing. Other researchers have also shown that chemical signals from the substrate and surrounding environment are important for directing the differentiation of adult stem cells into one tissue type or another. Scientists disagree, though, about whether adult stem cells are able to give rise to cells outside their own tissue family—for instance, whether a mesenchymal stem cell could generate liver cells.

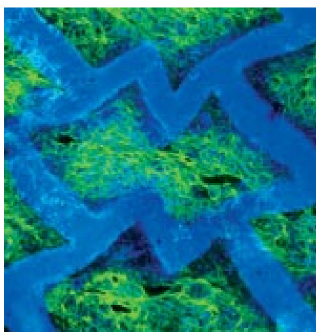
In contrast to adult stem cells, embryonic stem (ES) cells are easy to expand in culture and can differentiate into all the cell types of the human body. Langer, along with Shulamit Levenberg of the Technion-Israel Institute of Technology in Haifa and her colleagues, has demonstrated that ES cells can even be made to differentiate into a desired tissue type right on tissue-engineering scaffolds. This capability suggests the potential to make 3-D tissues on scaffolds directly from differentiating ES cells. These cells do present various challenges, however.

Directing the uniform differentiation of ES cells into the desired cell types is still quite difficult. In attempts to mimic the complex natural microenvironment of ES cells and to optimize their differentiation, investigators are testing many conditions simultaneously to find the right combination of cues from different materials and matrix chemicals. They are also screening various small molecules as well as signaling proteins to identify factors that control "stemness"—the cells' ability to give rise to differentiated progeny while remaining undifferentiated themselves, ready to produce more new cells as needed.

Those insights could also be applied to producing cells with the capabilities of embryonic cells but fewer of the drawbacks. Beyond the difficulties just outlined, scientists are still unable to predict the behavior of transplanted stem cells in patients. Undifferentiated ES cells can form tumors, for instance, creating a risk of cancer if the cells are not all successfully differentiated before transplantation. In addition, researchers have been making efforts to address the ethical issues associated with deriving ES cells from human embryos by exploring approaches to producing ES-like cells from nonembryonic sources.

In the past couple of years remarkable progress has been made in producing ES-like cells from regular adult body tissue, such as skin cells. These altered cells, known as induced pluripotent stem (iPS) cells, are emerging as an exciting alternative to ES cells as a renewable resource for tissue engineering. In 2007 Shiro Yamanaka, then at Kyoto University, and James A. Thomson of the University of Wisconsin–Madison first showed that cells of adult tissue can be transformed to a primitive iPS state by reactivating a number of genetic pathways that are believed to underlie stemness.

**Tissue engineers are looking to other fields for insights, including studies of developing tissues and regenerating wounds.**



**HONEYCOMB SCAFFOLD design (*blue*) guides the alignment of rat heart cells, whose contractile fibers are stained green above. Human heart muscle must contract and dilate some 300 million times over an average life span without tiring. To replicate mechanical cues that enhance the cells' contractile ability, Lisa E. Freed and George C. Engelmayr, Jr., both at the Massachusetts Institute of Technology, designed their scaffold to have accordianlike flexibility. They used a laser to cut the honeycombed pores in "biorubber," a unique elastic material developed by Yadong Wang and Robert Langer.**



Reintroducing as few as four master regulatory genes into adult skin cells, for instance, caused the cells to revert to a primitive embryonic cell type. The early experiments used a virus to insert those genes into the cells, a technique that would be too dangerous to use in tissues destined for patients. More recent research has shown that a safer nonviral technique can be adapted to activate the same repertoire of stemness genes and even that activation of just a single regulatory gene may be sufficient. The rapid progress in this area has tissue engineers hopeful that soon a patient's own cells, endowed with ES cell capabilities, could become the ideal material for building tissue constructs. And even as we experiment with these different cell types, tissue engineers are also refining our building methods.

## Architectural Advances

A decade ago researchers assumed that cells are smart: if we put the correct cell types in proximity to one another, they would "figure out" what to do to form their native tissues. To some degree, this approach is effective, but we now have a greater appreciation of the intricacy of signals exchanged among cells and their surroundings during organ and tissue development as well as during normal functioning, and we know the importance of providing a tailored environment in our constructs.

Further, every tissue in the body performs specific tasks that engineered replacements must be able to perform, and we are learning that replicating the underlying biology of the tissue in question as closely as possible is critical to generating tissues that can carry out their intended functions. In more complex organs, multiple cell types work in concert—in the liver, for instance, the cells' jobs include detoxification and nutrient breakdown. Thus, the microarchitecture of tissues and the positioning of cells relative to one another must be re-created in tissue-engineered constructs to reproduce the desired functionality.

Early tissue-engineering work used scaffolds made from assorted materials to try to replicate the 3-D shape of the tissue as well as crudely approximate this spatial cell organization. A number of advances in the past few years have enhanced the level of complexity of engineered tissues and reproduced the tissue environment more closely. For example, scaffolds have been made by removing all the cells from natural tissues, leaving only connective fibers. These shells can be used to grow engineered tissues that recreate a significant amount of the function of the original tissue. In one particularly impressive study, decellularized rodent heart scaffolds that were seeded with cardiac and endothelial cells produced cardiac muscle fibers and vascular structures that grew into a beating heart.

Assorted "printing" technologies can also be used to arrange cells precisely. By modifying standard ink-jet printers, engineers can dispense cells themselves or scaffold materials to generate tissues or frameworks onto which cells can be seeded. Mimicking the tissue's natural topography also helps to guide the cells, and another technology borrowed from the engineering world, electrospinning, can produce scaffolds that resemble the texture of natural tissue matrix. Very thin polymer fibers are spun to form weblike scaffolds, which provide cells with a more natural 3-D environment, and the chemical and mechanical features of the polymer materials can be finely manipulated. David Kaplan of Tufts University has fashioned similar scaffolds from silk materials that resemble spider webs to generate ligaments and bone tissues.

Because the biological, chemical and mechanical properties of hydrogels can be readily manipulated, the gels are proving useful for supporting and encasing cells while enhancing the function of the resulting tissues. Hydrogels containing live cells can be "printed" or otherwise arranged and layered to delineate correct tissue structure. One of us (Khademhosseini) has shown, for example, that hydrogel-encased cell aggregates can be molded into any number of complementary shapes [*see box on next page*], then pooled together to self-organize into a larger complex pattern. This technique could be used to replicate the natural organization of cells in a tissue such as the liver, which is made up of hexagonal structures that each contain toxin-filtering cells surrounding a central blood vessel.

Some gels are designed so that their polymers link together in response to ultraviolet light, making it possible to sculpt the desired construct shape and then solidify it by exposing all or parts of the construct to light. Kristi Anseth of the University of Colorado at Boulder and Jennifer Elisseeff of Johns Hopkins University have generated cartilage and bone tissue using such pho-

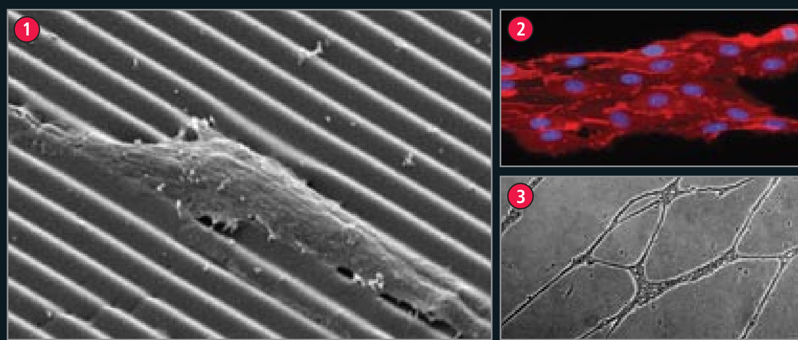
[TECHNIQUES]

# Building Blood Vessels

Living tissues quickly starve without the oxygen and nutrients delivered to cells by blood, so an engineered tissue construct that is more than a few cells thick usually requires an integrated vasculature. Endothelial cells form tiny capillaries and the interior lining of larger vessels within natural tissues, but coaxing endothelial cells to build a vascular network that penetrates an engineered tissue has been a major challenge. Nanoscale and microfabrication technologies borrowed from other fields, such as the semiconductor industry, are now allowing tissue engineers to control the cells' behavior and placement with unprecedented precision.

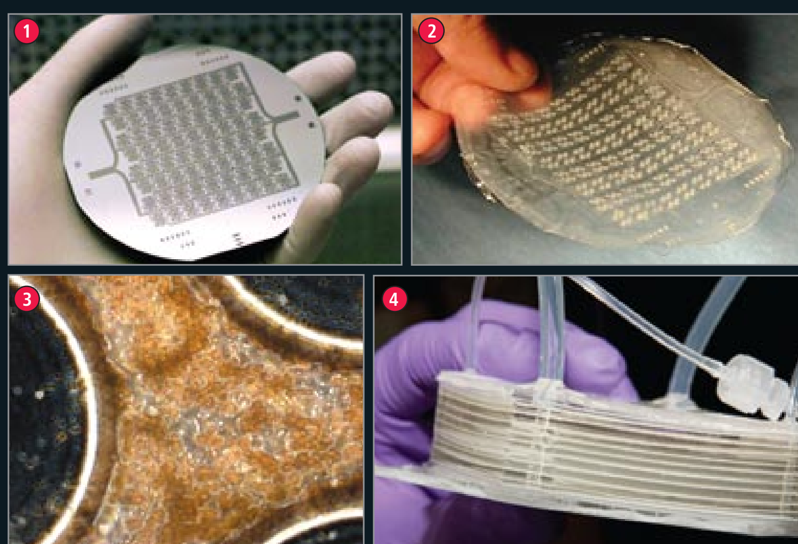
## NANOPATTERNED SURFACE

Cells respond to chemical signals from their neighbors and from the supportive extracellular matrix around them, but cells also respond to mechanical cues from the shape and texture of the surface on which they are growing. Grooves 600 nanometers (nm) deep and 1,200 nm wide mimic the natural matrix topography of certain tissues and provide endothelial cells with mechanical signals that affect the cells' shape and rate of migration and proliferation (*1*). After growing on the nanopatterned surface for six days, the cells multiply and align themselves in the direction of the grooves (*2*) and form a network of capillarylike tubes (*3*).



## MICROFABRICATION

To control the vasculature pattern within an implantable liver-assisting device, tissue engineers etch the desired blood vessel arrangement into a silicon mold (*1*). A biocompatible polymer scaffold cast from the silicon template (*2*) is then seeded with endothelial cells to coat the artificial vessel walls. Liver cells are cultured in the channels of similar scaffolds (*3*). Alternating layers of scaffolds containing "blood vessels" or liver cell cultures are stacked, with a nanoporous membrane between each layer, so that the liver cells are always close to the blood supply (*4*). The resulting hybrid tissue device, which has been tested in animals, is intended to serve as a bridge for patients awaiting a liver transplant.



COURTESY OF DRAPER LABORATORY (*1, top,* and *1* and *4, bottom*); "ENHANCEMENT OF IN VITRO CAPILLARY TUBE FORMATION BY SUBSTRATE NANOTOPOGRAPHY," BY C. J. BETTINGER, Z. ZHANG, S. GERECHT, J. T. BORENSTEIN AND R. LANGER, IN *ADVANCED MATERIALS*, VOL. 20; 2008 (*2* and *3, top*); "MICROSCALE TECHNOLOGIES FOR TISSUE ENGINEERING AND BIOLOGY," BY A. KHADEMHOSSEINI, R. LANGER, J. T. BORENSTEIN AND J. P. VACANTI, IN *PNAS*, VOL. 103, NO. 8; FEBRUARY 21, 2006. COPYRIGHT NATIONAL ACADEMY OF SCIENCES, U.S.A. (*2, bottom*); "THREE-DIMENSIONAL MICROFLUIDIC TISSUE-ENGINEERING SCAFFOLDS USING A FLEXIBLE BIODEGRADABLE POLYMER," BY C. J. BETTINGER, E. J. WEINBERG, K. M. KULIG, J. P. VACANTI, Y. WANG, J. T. BORENSTEIN AND R. LANGER, IN *ADVANCED MATERIALS*, VOL. 18; 2006 (*3, bottom*)

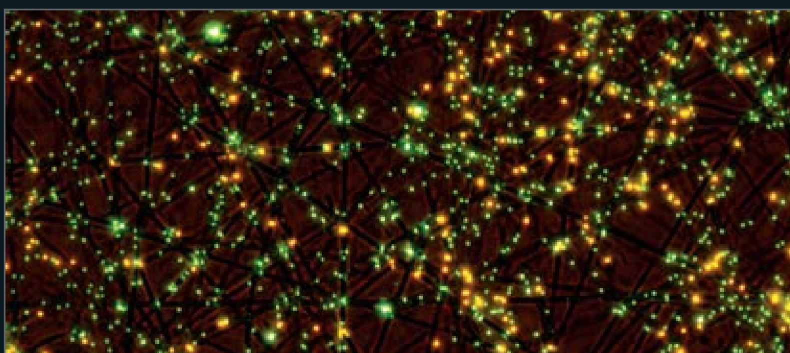
[TECHNIQUES]

# Advanced Building Materials

Engineers want to reproduce the internal structure of a natural tissue as closely as possible because cells depend on environmental cues to maintain themselves and to do their jobs. New techniques and materials are giving tissue engineers finer control and faster methods of creating cell constructs designed to grow into a functioning implant.

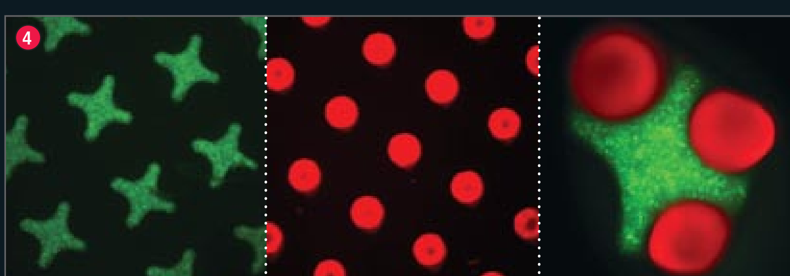
## ELECTROSPINNING FIBERS

A manufacturing technique for producing ultrafine fibers—nanometers or microns in diameter—from liquids and other substances has recently been adapted to produce meshlike cell scaffolds. This type of surface maximizes the space available for cells and the cells' contact with the scaffolding material itself—which mimics the texture of extracellular matrix and can be imbued with growth-promoting chemicals. Such scaffolds have been made from silk and a variety of polymers. Living cells can even be incorporated within the fibers themselves (*green dots*) to ensure they are evenly distributed throughout the scaffold.



## ASSEMBLING HYDROGELS

Suspending living cells within polymer hydrogels allows tissue engineers to create cell arrangements that mimic natural tissue structure. Polymer molecules link to one another in response to ultraviolet light, causing the gel to stiffen enough to be sculpted into building blocks and assembled into larger patterns. A method for producing self-assembling hydrogel-cell blocks begins with a hydrophilic (water-loving) gel formulation that is laden with live cells and made into cubes using photolithography (*1*). When the blocks are suspended in oil and agitated, the hydrophilic units are drawn to one another, forming larger aggregates that can be stabilized by a second cross-linking light exposure (*2*). Cells (*green*) remain viable within the blocks (*3*). Dye-containing blocks illustrate how hydrogel units carrying different types of cells could be shaped to self-assemble into larger constructs mirroring natural tissue structures such as liver sinusoids (*4*).


tocrosslinkable hydrogels. Gels can also be imbued with a number of signaling molecules to promote tissue growth or differentiation. Samuel Stupp of Northwestern University has shown that neural stem cells differentiate into neurons within a hydrogel that incorporates small proteins that act as environmental signals directing the cells' behavior. Helen M. Blau of Stanford University has also used hydrogels containing extracellular matrix components to control and study the properties of individual stem cells.

Finally, nanotechnology has been enlisted to generate engineered sheets of cells suitable for transplantation. Teruo Okano of Tokyo Women's Medical University has produced surfaces coated with a temperature-responsive polymer that swells as the temperature is lowered from 37 to 20 degrees Celsius. Cells are first induced to form a single layer on these nanoengineered surfaces, then the temperature is lowered to swell the underlying substrate and detach the intact cell sheet. These cell sheets, which contain appropriate cell-secreted matrix molecules can then be stacked or rolled to build larger tissue constructs.

Although these advances have made a significant improvement in the range and diversity of scaffolds that can be generated, challenges persist in this area as well. One difficulty is a lack of knowledge of the concentrations and combinations of growth factors and extracellular molecules that are present at specific stages of development and wound healing in various tissues. A better understanding of these design parameters is needed to engineer tissues that mimic the body's own healing and development. Thus, tissue engineers are looking to other fields for insights, including studies of gene and protein interactions in developing tissues and regenerating wounds. Incorporating these findings with advanced culture systems is helping us to better control the responses of cells outside the body, but more progress is needed.

## Coming of Age

Despite the ongoing challenges we have described, engineered tissues are no longer a fantastical prospect. Simple manufactured tissues are already in clinical use, and this method of restoring or replacing biological function is now poised to become a viable therapy for millions of patients in need. As of late 2008, various tissue-engineered products generated annual sales of nearly $1.5 billion.

Those figures are all the more impressive in light of setbacks to the field that occurred short-

COURTESY OF SUWAN JAYASINGHE (*electrospinning*); "DIRECTED ASSEMBLY OF CELL-LADEN MICROGELS FOR FABRICATION OF 3D TISSUE CONSTRUCTS," BY YANAN DU, EDWARD LO, SHAMSHER ALI AND ALI KHADEMHOSSEINI, IN *PNAS*, VOL. 105, NO. 28; JULY 15, 2008. COPYRIGHT NATIONAL ACADEMY OF SCIENCES, U.S.A. (*1–4*)

# A FULL PIPELINE

At least 70 companies have developed or are developing implantable tissue-engineered products, meaning that they replace or restore human tissue function by combining engineering principles and materials with living cells. In many of the most commercially advanced products, those cells are supplied by the patient destined to receive the implant. These include a variety of cell-free scaffold materials intended to foster regeneration by the patient's own tissues, as well as cell grafts and aggregations. Whole tissues can include large engineered blood vessels and other implants that completely replace the patient's original tissue, as well as many types of complex skin used for patient grafts and, increasingly, for animal-free testing of chemicals.

| | EXAMPLES OF COMPANIES AND STAGE OF PRODUCT DEVELOPMENT | | |
|---|---|---|---|
| IMPLANT TYPE | Preclinical | Clinical Trials | Approved |
| **Cell-free supports** (Implantable or injectable scaffold materials and tissue matrix components) | 3DM, Cardio, Cytomatrix, RegenTec, Regentis Biomaterials, Tepha | Celltrix, Forticell Bioscience, Kuros Biosurgery, Serica Technologies | Advanced Biopolymers, Baxter, Cook Biotech, Fidia, Imedex Biomateriaux, Integra, Johnson & Johnson, Lifecell, Medtronic, Orthovita, Pioneer Surgical Technology, ReGen Biologics, TEI Biosciences, Tissue Regeneration Therapeutics |
| **Cell-based products** (Encapsulated cells, single-cell-type aggregations or sheets, organ-assist devices) | BioEngine, Cerco Medical, GeneGrafts, MicroIslet | ArBlast, Excorp, HepaLife Technologies, Isolagen, LCT, Neurotech, Novocell, NsGene, Pervasis Therapeutics, TiGenix, Vital Therapies | Advanced BioHealing, Arthro Kinetics, Biotissue Technology, Cell Matrix, CellTran, Genzyme, Hybrid Organ, Interface Biotech, Organogenesis, SEWON Cellontech, Tetec, Vasotissue Technologies |
| **Whole tissues** (Blood vessels, cartilage, bone, bladder, heart muscle, complex skin) | Bio Nova, Humacyte | BioMimetic Therapeutics, Cytograft, Educell, Histogenics, Intercytex, ISTO, Tengion, Theregen | Euroderm, Japan Tissue Engineering, Karocell Tissue Engineering, MatTek, Skin Ethic Laboratories |

ly after we last wrote for this magazine about the promise of tissue engineering. At the end of the 1990s and into the early 2000s, enthusiasm and investment were high, but with the burst of the Internet financial bubble, funding for biotechnology start-ups dwindled. Even companies with tissue-engineered products approved by the Food and Drug Administration had to restructure their business models, delaying introduction of their products to the market. Because engineered tissues are made from cells, biologically active chemicals and nonbiological scaffold materials, the constructs must undergo rigorous analysis by the FDA, which is costly and time-consuming. A lack of funding made conducting extensive clinical trials more difficult for companies. Ironically, the delay in commercializing some tissue-engineered products had an upside—it bought time for the science to mature and for business approaches to become more sophisticated.

There is still room for improvement. Obtaining FDA approval is still a major hurdle, in part because cells obtained from different people may not behave alike and because recipients can have varying responses to the same kind of implant. Such unpredictability can make it difficult for the FDA to determine that a given engineered construct is safe and effective. Further research is therefore important to measure and understand variations between individuals and to account for them in clinical trials that study tissue-engineered products. And future business models must include the extensive costs that will be associated with this work.

Still, armed with recent insights into how tissues develop and how the body repairs itself naturally, tissue engineers are now aiming to create second-generation products that are closer mechanically, chemically and functionally to their biological counterparts than ever before. Even in today's strained economic climate, we expect that research into nanotechnology, stem cell biology, systems biology and tissue engineering will soon converge to yield fresh ideas for devising the sophisticated organ substitutes needed by so many people today. ■


**[THE AUTHORS]**

**Ali Khademhosseini** is an assistant professor at Harvard-MIT's Division of Health Sciences and Technology and at Harvard Medical School. Since earning his Ph.D. under Langer's direction, Khademhosseini has focused his research on developing microscale and nanoscale technologies to control cellular behavior for tissue engineering and drug delivery. **Joseph P. Vacanti** is surgeon in chief at Massachusetts General Hospital for Children, a professor at Harvard Medical School, and deputy director of the Center for Regenerative Medicine at Massachusetts General Hospital. **Robert Langer** is an Institute Professor at the Massachusetts Institute of Technology and the most cited engineer in history. Langer and Vacanti pioneered tissue-engineering research together and wrote about their fledgling field in the September 1995 and April 1999 issues of *Scientific American.*

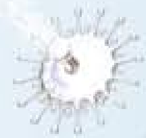

## MORE TO EXPLORE


**Bringing Safe and Effective Cell Therapies to the Bedside.** Robert A. Preti in *Nature Biotechnology,* Vol. 23, No. 7, pages 801–804; July 2005.

**Microscale Technologies for Tissue Engineering and Biology.** Ali Khademhosseini, Robert Langer, Jeffrey Borenstein and Joseph P. Vacanti in *Proceedings of the National Academy of Sciences USA,* Vol. 103, No. 8, pages 2480–2487; February 21, 2006.

**Engineering Complex Tissues.** Antonios G. Mikos et al. in *Tissue Engineering,* Vol. 12, No. 12, pages 3307–3339; December 2006.

**Great Expectations: Private Sector Activity in Tissue Engineering, Regenerative Medicine, and Stem Cell Therapeutics.** Michael J. Lysaght et al. in *Tissue Engineering,* Part A, Vol. 14, No. 2, pages 305–315; February 2008.



# POWERING NANOROBOTS

Catalytic engines enable tiny swimmers to harness fuel from their environment and overcome the weird physics of the microscopic world

By Thomas E. Mallouk and Ayusman Sen

**KEY CONCEPTS**

- Nanotechnology promises futuristic applications such as microscopic robots that assemble other machines or travel inside the body to deliver drugs or do microsurgery.
- These machines will face some unique physics. At small scales, fluids appear as viscous as molasses, and Brownian motion makes everything incessantly shake.
- Taking inspiration from the biological motors of living cells, chemists are learning how to power microsize and nanosize machines with catalytic reactions. *—The Editors*

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

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

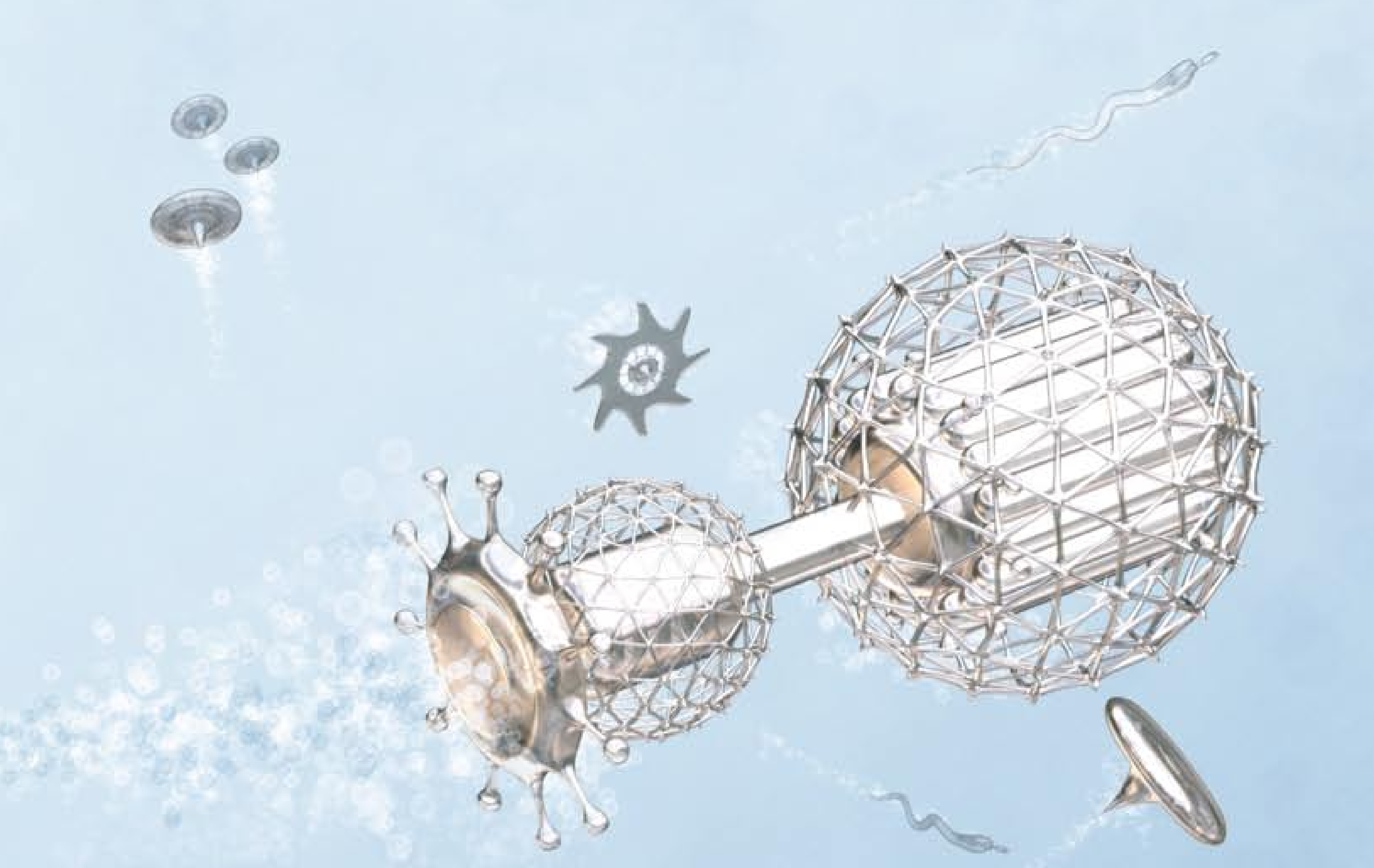
But look under the hood of the nanocar, and you will not find an engine. Tour's nanocars so far move only insofar as they are jostled by random collisions with the molecules around them, a process known as Brownian motion. This is the biggest current problem with molecular machines: we know how to build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

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

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

In 2004 we were part of a team at Pennsylvania State University that developed simple nanomotors that catalytically con-

KENN BROWN *Mondolithic Studios (microscopic robots)*



vert the energy stored in fuel molecules into motion. We took inspiration from a considerably larger catalytic motor reported in 2002 by Rustem Ismagilov and George Whitesides, both at Harvard University. The Harvard team had found that centimeter-scale "boats" with catalytic platinum strips on their stern would spontaneously move on the surface of a tank of water and hydrogen peroxide ($H_2O_2$). The platinum promoted the breakup of $H_2O_2$ into oxygen and water, and bubbles of oxygen formed that seemed to push the boats ahead by recoil, the way the exhaust coming out the back of a rocket gives it forward thrust.

## Credible Shrinking

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

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

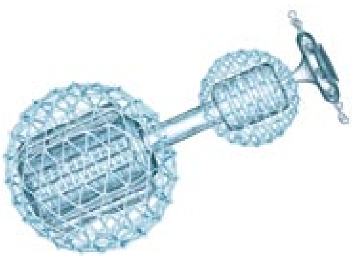
At the macroscale, the notion of recoil makes good sense. When someone swims or rows a boat, their arms, legs or oars push water backward, and the recoil force pushes the body or boat forward. In this way, a swimmer or boat can glide forward even after one stops pushing. How far an object glides is determined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

**MICROSCOPIC ROBOTS of the future (shown here in an artist's conception) may have finally found a source of power. Engines that convert chemical energy into motion could someday enable swimming nanomachines to operate despite the random motion and fluid thickness that tend to dominate at microscopic scales.**

SCI AM
**See Videos ...**
Watch footage of nanoswimmers at **www.SciAm.com/nanomotor**

**[THE AUTHORS]**

**Thomas E. Mallouk** is DuPont Professor of Materials Chemistry and Physics at Pennsylvania State University. His research focuses on the synthesis and properties of nanoscale inorganic materials. **Ayusman Sen**, who was born in Calcutta, India, is professor of chemistry at Penn State. His research focuses on catalysis and inorganic and organic materials. Sen numbers enological and gastronomical explorations among his favorite pastimes. The authors first realized in a casual conversation that Sen's idea for a catalytic motor could be effected with nanorods that had already been made in Mallouk's laboratory.



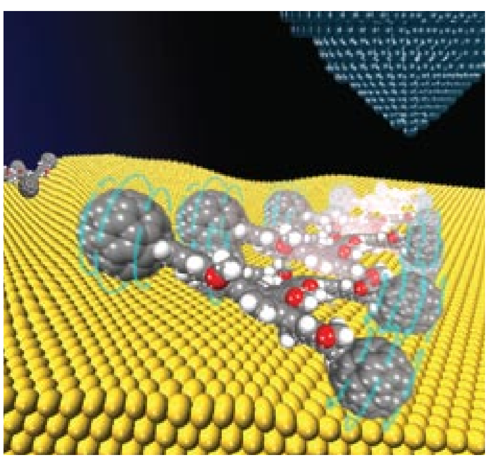
after the recoil from bubbles) are hopeless.

The way our nanorods actually work is that they apply a continuous force to prevail over the drag with no need for gliding. At the platinum end, each $H_2O_2$ molecule is broken down into an oxygen molecule, two electrons and two protons. At the gold end, electrons and protons combine with each $H_2O_2$ molecule to produce two water molecules. These reactions generate an excess of protons at one end of the rod and a dearth of protons at the other end; consequently, the protons must move from platinum to gold along the surface of the rod.

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

Once this principle was established (with the help of our students and our Penn State collaborators Vincent H. Crespi, Darrell Velegol and Jeffrey Catchmark), several other catalytic nanomotor designs followed. And Adam Heller's research group at the University of Texas at Austin and Joseph Wang's group at Arizona State University showed that mixtures of different fuels—glucose and oxygen or $H_2O_2$ and hydrazine—could make motors run faster than they do with a single fuel.

Whereas freely suspended metal nanorods move with respect to the bulk solution, an immobilized metal structure in the presence of $H_2O_2$ will induce fluid flows at the interface between the structure and the fluid, thereby potentially powering the motion of something else immersed in the fluid. We have demonstrated this fluid-pumping effect on a gold surface patterned with silver.



NANOCAR is one of several types of synthetic molecular-scale machines with moving parts. It has carbon-based axles and four wheels consisting of buckyballs—carbon molecules shaped like soccer balls. So far, however, the nanocar lacks an engine, so it just moves back and forth randomly when the surface heats up (*arrows*).

## Steering Committee

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

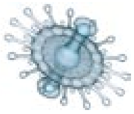
Our first attempt to solve the steering problem relied on a magnetic field [*see box on page 76*]. We embedded nickel disks in the rods. These disks react to magnetic fields like tiny compasses with their north-pole to south-pole axes perpendicular to the length of the cylinders. A refrigerator magnet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

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

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

Our nanomotors move faster at higher con-

COURTESY OF THE AUTHORS (*Mallouk and Sen*); T. SASAKI *Rice University* (*nanocar*) centrations of fuel, and this tendency effectively lengthens their straight runs. Consequently, they move on average toward a source of fuel, such as a gel particle soaked with hydrogen peroxide [*see photographs on next page and video online*].

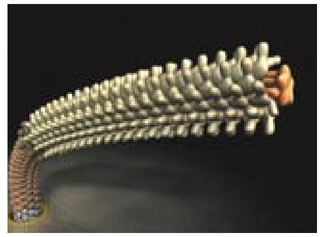


More recently, the two of us have also demonstrated motor particles that are driven by light, or phototaxis. These particles use light to break up molecules and create positive and negative ions. The two types of ions diffuse away at different speeds, setting up an electric field that causes the particles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

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

## Scaling Down

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

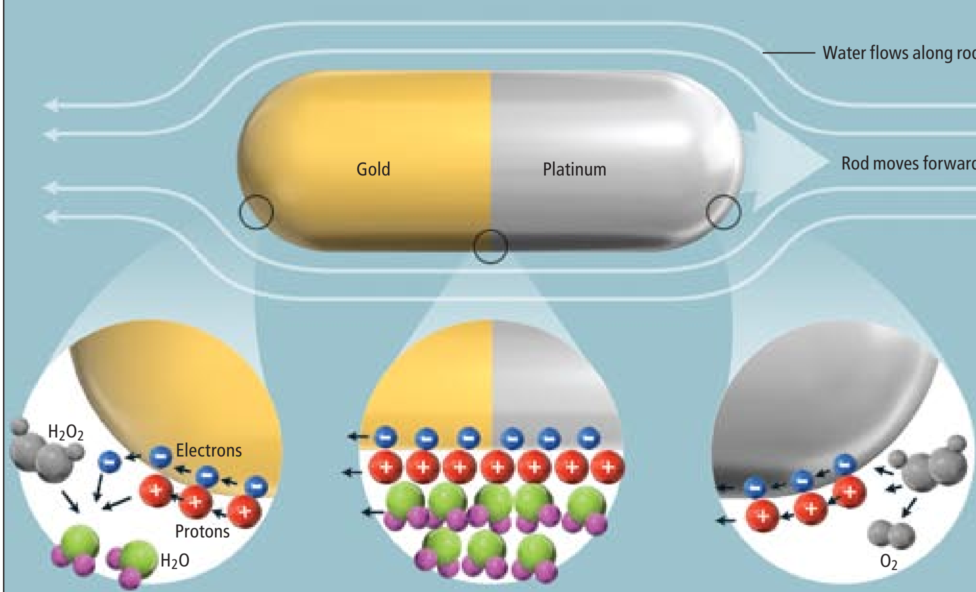


**NATURAL-BORN SWIMMERS:** Bacteria such as *Escherichia coli* use molecular motors to twist tail-like filaments called flagella; above, a computer model depicts a flagellum's molecular structure. The turning pushes the cell forward, a bit like untwisting a screw counterclockwise draws it up. In a bacterium's liquid environment, viscosity dominates over inertia, so if the flagella stop turning, the bacterium comes to a stop almost instantly.

[HOW IT WORKS]

## ANATOMY OF A CATALYTIC ENGINE

The authors created two-micron-long gold-platinum rods that propel themselves in a solution of water and hydrogen peroxide ($H_2O_2$) by pushing the fluid along their sides. The fluid's flow is powered by two different chemical reactions occurring at the gold and platinum surfaces (*insets*). The uninterrupted flow enables the rods to overcome the fluid's viscosity. Catalytic engines could help bacterium-sized robots navigate inside the human body, and can drive microscopic machine parts such as gears (*micrograph at far right*).




**1 PROTONS NEEDED**
The gold surface catalyzes a reaction that takes protons, electrons and $H_2O_2$ and produces $H_2O$. The reaction calls for protons and electrons to flow in from the platinum side.

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

**3 PROTONS PRODUCED**
The platinum surface continuously generates the needed protons by catalyzing the breakdown of $H_2O_2$ into electrons, protons and $O_2$.


**ROTARY MOTOR**
The same pair of chemical reactions moves protons and water around the teeth of this 100-micron-wide wheel, making it turn.

KEIICHI NAMBA *Osaka University* AND ERATO PROTONIC NANOMACHINE PROJECT, JST (*flagellum*); SOURCE: "DIRECTED ROTATIONAL MOTION OF MICROSCALE OBJECTS USING INTERFACIAL TENSION GRADIENTS CONTINUALLY GENERATED VIA CATALYTIC REACTIONS," BY JEFFREY CATCHMARK, SHYAMALA SUBRAMANIAN AND AYUSMAN SEN, IN *SMALL*, VOL. 1, NO. 1; 2005 (*nanomotor*)

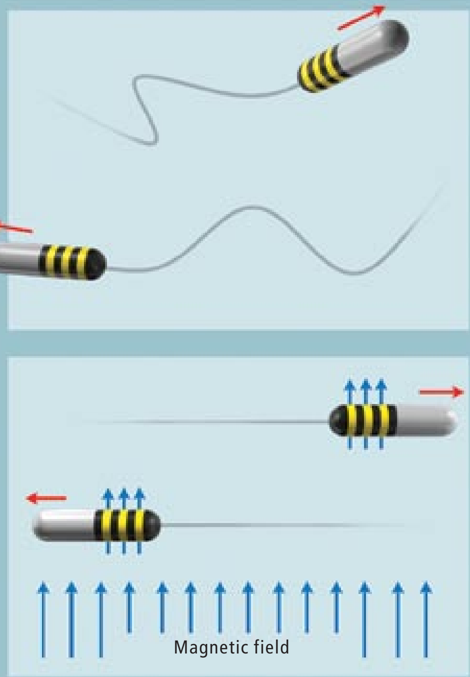
[STEERING 101]

## COMPASS NAVIGATION

For nanorobot mobility, finding suitable propulsion is only half of the problem. Another challenge is to keep the robots going in a steady direction and to steer them to their destination. Special nanorods with built-in compasses (with north-south axis straddling the rod's width) allow for magnetic steering.

**UNCONTROLLED RODS**
When the magnetic field is off, motion is random.

**STEERABLE RODS**
Turning on the magnetic field orients the rods perpendicular to the field. The rods then move in just one direction, which can be controlled by reorienting the magnetic field.




should be about proportional to its linear size (the dimensions such as length or width). This scaling law follows from the fact that the drag force is proportional to size, and the rate of catalytic reaction is proportional to the surface area, which goes as the *square* of the size.

Penn State biologist James H. Marden has found a more general scaling law, relating the mass of a motor and the maximum force it can exert. The upshot of his law, which holds for molecular motors all the way up to jet engines, is that smaller motors are always slower. In terms of the ultimate scaling of catalytic nanomotors, there comes a point (around 50 to 100 nanometers) when Brownian motion swamps out any propulsion from the catalytic reaction. As a consequence, micron-size bacteria are the smallest free swimmers in all of biology. At smaller scales, Brownian motion makes it all but impossible to keep a steady direction of motion while immersed in a fluid. In fact, all molecular-scale motors in nature—including muscle proteins and the enzymes that produce ATP—are either constrained to run along a track or embedded in a membrane. The same will have to be true of any future molecular-scale robots.

### Ratcheting Up

For molecular-scale motors, simple surface catalysis as demonstrated in our nanorods may also be too inefficient to counter Brownian motion, whether or not the robot's motion is constrained. Nature, however, has found ways to put Brownian motion to work rather than fighting it. Many biological motors are based on the principle of the Brownian ratchet, which uses energy from chemical catalysis not to create motion in a certain direction but to allow Brownian-motion jolts only when they push in the favorable direction, while blocking them when they push in the opposite direction [see "Making Molecules into Motors," by Dean Astumian; Scientific American, July 2001]. In recent years researchers have started experimenting with the first artificial Brownian ratchets [*see box on opposite page*].

Another approach to propulsion and steering has been demonstrated by Orlin Velev of North Carolina State University and his collaborators. These researchers have recently shown how to propel objects in fluids without any fuel. Their vessels contain a diode, a device that allows electric currents to cross it in one direction but not in the opposite direction. The researchers apply an alternating electric field. In the vicinity of the vessel, the diode converts the alternating field into a static one. The static field points in a constant direction, producing a net force that provides a thrust.

Because they are externally powered, diode motors turn out to follow a different scaling law than catalytic motors. Velev has demonstrated

**BREAD CRUMB TRAIL:** Catalytic nanorods tend to move in random bursts in the presence of fuel, but the bursts last longer where the fuel concentration is higher. The net effect is that the nanorods move up the fuel's chemical gradient much as bacteria track down food by following its scent. Here the rods are seen congregating around fuel-soaked gel (*upper left in each frame*).

SOURCE FOR BOX: "CHEMICAL LOCOMOTION," BY WALTER F. PAXTON, SHAKUNTALA SUNDARARAJAN, THOMAS E. MALLOUK AND AYUSMAN SEN, IN *ANGEWANDTE CHEMIE INTERNATIONAL EDITION*, VOL. 45, NO. 33; 2006; DON FOLEY (*illustration*); "CHEMOTAXIS OF NON-BIOLOGICAL COLLOIDAL RODS," BY YIYING HONG, NICOLE M. K. BLACKMAN, NATHANIEL D. KOPP, AYUSMAN SEN AND DARRELL VELEGOL, IN *PHYSICAL REVIEW LETTERS*, VOL. 99, NO. 17; OCTOBER 2007 (*chemotaxis series*)

[MOLECULAR-SCALE MOTORS]

# FREE LUNCH (AT A COST)

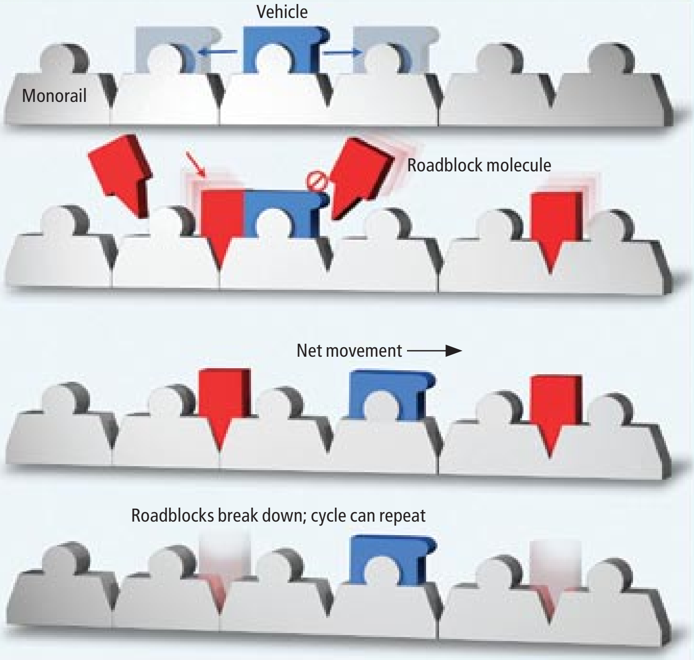
Molecules are never completely still. In the case of a liquid, the random movement is known as Brownian motion. Chemists are creating the first artificial Brownian ratchets, molecular-scale machines that harness Brownian motion rather than fight against it. David Leigh of the University of Edinburgh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

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

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

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

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




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

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

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

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

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

DON FOLEY

## MORE TO EXPLORE

**Life at Low Reynolds Number.** E. M. Purcell in *American Journal of Physics,* Vol. 45, No. 1, pages 3–11; January 1977.

**Molecules, Muscles and Machines: Universal Performance Characteristics of Motors.** James H. Marden and Lee R. Allen in *Proceedings of the National Academy of Sciences USA,* Vol. 99, No. 7, pages 4161–4166; April 2, 2002.

**Chemical Locomotion.** Walter F. Paxton, Shakuntala Sundararajan, Thomas E. Mallouk and Ayusman Sen in *Angewandte Chemie International Edition,* Vol. 45, Issue 33, pages 5420–5429; August 18, 2006.

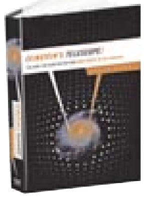
**Can Man-Made Nanomachines Compete with Nature Biomotors?** Joseph Wang in *ACS Nano,* Vol. 3, No. 1, pages 4–9; January 27, 2009.

# Dark Universe ▪ Manhattan circa 1609

**BY MICHELLE PRESS**

### ➔ EINSTEIN'S TELESCOPE: THE HUNT FOR DARK MATTER AND DARK ENERGY IN THE UNIVERSE

by Evalyn Gates. W. W. Norton, 2009 ($25.95)



Not so long ago, Gates begins, astrophysicists, thrilled with bigger and better telescopes, "settled in to appreciate the unprecedented clarity of their view of the cosmos, only to find that their new instruments revealed a Universe that didn't act at all the way it was supposed to." Instead their observations insisted that the stars and galaxies we see are only a small part of the matter that exists. The remainder, composed of new kinds of particles called dark matter and the even stranger dark energy, is invisible to their telescopes.

Fortunately, as Gates (an astrophysicist at the University of Chicago) details, scientists can use space itself as a telescope to search for dark matter and dark energy. According to Einstein, mass of any kind warps space: just as every planet and star creates a "dimple" in space, so

## EXCERPT

### ➔ MANNAHATTA: A NATURAL HISTORY OF NEW YORK CITY

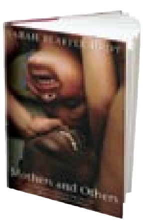
by Eric W. Sanderson. Illustrations by Markley Boyer. Abrams, 2009 ($40)

*Using a detailed map created by the British army in about 1782, Sanderson, a landscape ecologist at the Wildlife Conservation Society, re-creates Manhattan as it would have looked when Henry Hudson first saw it in 1609* (left side of image)*. The goal is not to return today's Manhattan* (right side of image) *to its primeval state but to have some fun and to see what vision of the future might work for the metropolis.*

"... we can literally reconstruct the view out of any office building or apartment in Manhattan as it appeared four hundred years ago. Using computer techniques borrowed from the moviemakers, we place trees and streams according to scientific probability distributions, true to the ecology and the landscape, and faithful to the geography of the city, block by block, street by street. These images show us nature in all her beauty, complexity, and loveliness at a time before streets and blocks and tall buildings, before the human footprint lay so heavily on Manhattan and the world."

COPYRIGHT © MARKLEY BOYER/THE MANNAHATTA PROJECT/WILDLIFE CONSERVATION SOCIETY (*left*); COPYRIGHT © YANN ARTHUS-BERTRAND/CORBIS (*right*); COMPOSITE IMAGE BY MARKLEY BOYER dark matter also deforms the space around it. This warping acts as a gravitational lens—the "telescope" of the book's title—to bend and deflect light in the same way that lenses made of glass or plastic do. Using gravitational lensing, scientists have already discovered extrasolar planets and black holes and have reconstructed the collision of two giant clusters of galaxies. Researchers now have the potential, Gates maintains, to unveil dark matter and dark energy and to find new clues to the mystery of what the universe is made of.

**➔ MOTHERS AND OTHERS: THE EVOLUTIONARY ORIGINS OF MUTUAL UNDERSTANDING**
by Sarah Blaffer Hrdy. Harvard University Press, 2009 ($29.95)



More than a million years ago, somewhere in Africa, a group of apes began to rear their young differently. Unlike almost all other primates, they were willing to let others share in the care of infants. The reasons for this innovation are lost in the ancient past, but according to well-known anthropologist Hrdy, it was crucial that these mothers had related—and therefore trusted—females nearby and that the helpers provided food as well as care. Out of this "communal care," she argues, grew the human capacity for understanding one another: mothers and others teach us who will care and who will not. Beginning with her opening conceit of apes on an airplane (you wouldn't want to be on this flight) and continuing through her informed insights into the behavior of other species, Hrdy's reasoning is fascinating to follow.

Readers interested in this topic might also want to look at two other books just out: *On Kindness*, by Adam Phillips and Barbara Taylor (Farrar, Straus and Giroux, $22), and *The 10,000 Year Explosion*, by Gregory Cochran and Henry Harpending (Basic Books, $27).

# *How does* **food irradiation** *work? Is it safe?*

**Sam Beattie,** a food science professor at Iowa State University, zaps a reply (as told to Jordan Lite):

Irradiation treatments expose food to a dose of ionizing radiation, which disrupts the DNA or proteins of bacteria that make people ill.

Anytime you break bonds in chemicals you are bound to introduce changes, so it is critical that those alterations do not impart any toxicological effects to the food. Irradiation appears to be safe in that sense. The process does produce some unique by-products, but no evidence exists that these cause human illness at the levels found in irradiated food. There was some thought that 2-alkylcyclobutanone, a by-product derived from a fatty acid, could cause cell mutations that might lead to cancer, but the most recent findings suggest otherwise.

Two primary sources provide irradiation: radioactive elements—such as cobalt 60—and the electron beam, or e-beam. Cobalt 60 is an isotope, a traceable radioactive version of the element, that emits gamma rays, whereas the e-beam is an electron-based source. Cobalt 60 has a lower dose rate, so it takes longer—a span of minutes. The e-beam is more intense, with a higher dose rate, so it works in a matter of seconds. We are also experimenting with x-rays as a potential new approach.

In the U.S., irradiation is not as common as it is in some other countries, where preventing spoilage is an important contributor to food security. Among fresh produce, the Food and Drug Administration has approved irradiation to reduce food-borne illness only in leaf spinach and iceberg lettuce. For other food management purposes, however, it is approved for a variety of foods. On imported produce, for instance, irradiation can be employed to knock out pests or to control sprouting and ripening. With meat, it is an approved pasteurization process for killing organisms such as *Escherichia coli* or *Salmonella*.

Irradiation is not a blanket treatment. Practitioners tune the dosage and duration for the pathogen that is riskiest and most likely to be found in a given food. In pasteurizing meat, for instance, the radiation might be targeted to kill *E. coli* rather than *Clostridium botulinum* spores, which produce the toxin that causes botulism, because *E. coli* is more likely to be present and to cause problems. Irradiation does not work as well against viruses, although viruses typically appear in food service settings, where personal hygiene comes into play, rather than in processed foods.

Although irradiation is effective in many circumstances, it would not necessarily have prevented the recent *Salmonella* outbreak in peanut butter. Products high in fat are not as amenable to the treatment, because fats produce unwanted flavors when they break down. After *Salmonella* outbreaks in 2001 and 2004, the U.S. Department of Agriculture now requires California almonds to be heat-pasteurized or chemically treated. Peanuts are likely to see similar regulation mandating a thermal process—roasting in dry heat or immersion in hot oil.


ANTHONY-MASTERSON *Digital Vision/Getty Images (basket of strawberries)*; U.S. DEPARTMENT OF AGRICULTURE, FOOD SAFETY AND INSPECTION SERVICE *(radura symbol)*; SCIENTIFIC AMERICAN *(photoillustration)*

# *Indoor plants tend to grow toward the light, so why do* **trees outdoors grow straight** *instead of leaning toward the equator?* —W. Anderson, Sacramento, Calif.

**Edgar Spalding,** a botany professor at the University of Wisconsin–Madison, sprouts off:

A plant on a windowsill experiences a stronger light gradient than does a tree outdoors, where gravitational cues can overpower more subtle light-direction cues. Indoor plants get a lot more light on one side than on the other, which activates photoreceptor molecules to a much greater extent on the lit side. This difference is biochemically translated as a growth response, known as phototropism, which makes the plant bend toward the light.

Trees growing at a latitude of, say, 60 degrees are also asymmetrically illuminated because of the slant of the noon sun—approximately 55 degrees at the beginning of the summer growth season—but the difference in light intensity there is smaller and more variable. The modest light gradient experienced by the tree is counteracted by a continuous gravitational influence, known as gravitropism, which guides plant growth upward. The strength of gravitropism trumps phototropism in the tree scenario but not on the windowsill.

The edge of forest gaps provides a good place to observe light-guided tree growth at any latitude. There the effect of a strong light gradient can be seen in the reaching of trees into the gap. ■

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