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SCIENTIFIC AMERICAN

New Concerns about **FLUORIDE**
page 74

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A GRAND PLAN FOR SOLAR ENERGY

By 2050 it could free the U.S. from foreign oil and slash greenhouse emissions. Here's how ...

Nanotech Power

Tiny Devices Reclaim Wasted Energy

Cancer Drug Paradox

It Kills Tumors by Repairing Them

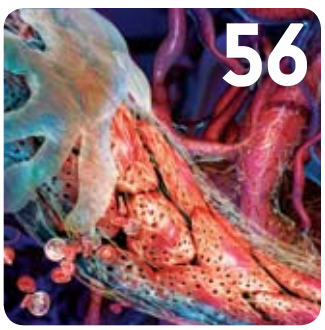
Sing Out!

The Physics of the Voice

FEATURES

SCIENTIFIC AMERICAN January 2008 ■ Volume 298 Number 1

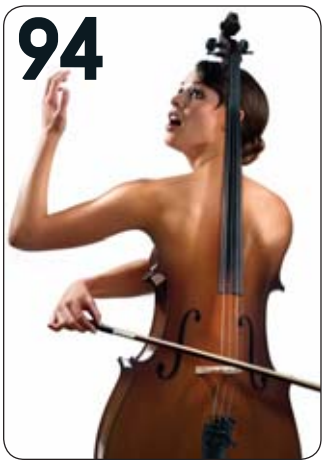
IMAGE BY KENN BROWN



ON THE COVER

Solar power is sometimes dismissed as too expensive or impractical. Yet with sufficient commitment and investment, it could become the major source of electricity in the U.S. Image by Jean-Francois Podevin. Photograph of toothbrush by Smitha Alampur.

MORE FEATURES



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RECORD-SETTING STELLAR BLACK HOLE ▼

Scientists uncovered the newly crowned champ, shown here stealing gas from its neighboring blue star. More at **www.SciAm.com/ontheweb**

AURORE SIMONNET *Sonoma State University/NASA*

In Focus

Hospitals and Superbugs: Go in Sick … Get Sicker

Nearly 100,000 people die every year from preventable infections they pick up in health care facilities.

News

Can a Lack of Sleep Cause Psychiatric Disorders?

Study shows that sleep deprivation leads to a rewiring of the brain's emotional circuitry.

Podcast

Mom's Baby Talk Crucial for Baby

Adults have to engage in baby talk, regardless of the language they speak, so that babies can learn to talk like adults.

Blog

Video of a Sphere Turning Inside Out without Creasing

Check out *Outside In,* an animation that shows how to "evert" a sphere.

Strange but True

Snake Oil Salesmen Were On to Something

Snake oil really is a cure for what ails you, if that happens to be arthritis, heart disease or maybe even depression.

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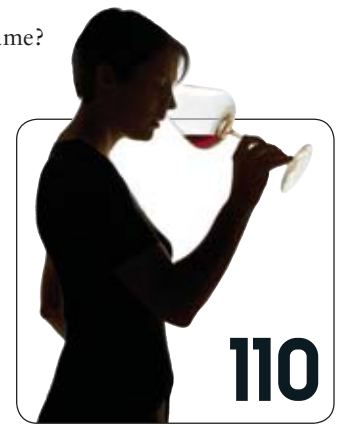

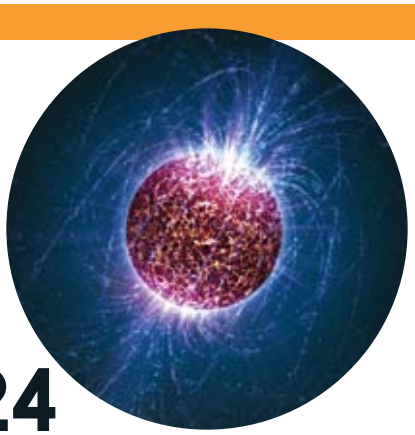

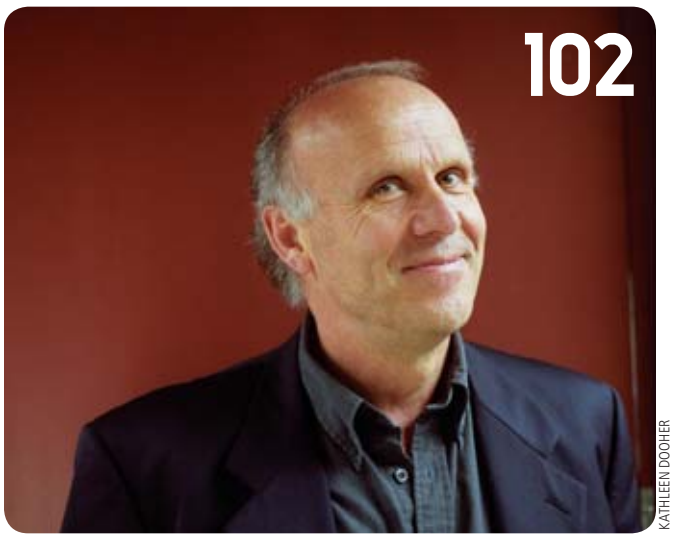

KATHLEEN DOOHER

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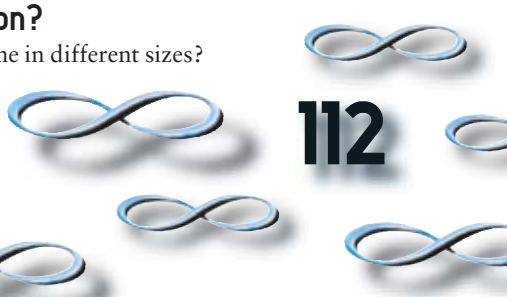
Featured Q & A
Read an interview with Richard Wrangham at **www.SciAm.com/ontheweb**



Big and Small Solutions

Meeting U.S. energy challenges requires more than one kind of ambition

With oil nearing $100 a barrel and atmospheric greenhouse gas concentrations steadily rising, the U.S. must commit seriously to a long-term plan that will improve the nation's energy security and address climate change threats. To date, national leaders have expended a lot of rhetoric on the importance of those goals, but relative to the country's magnitude as both a consumer of energy and a producer of carbon dioxide, they have taken few meaningful steps to reach them. The U.S. needs to get off the sidelines and put some skin into the game.

HOW BRIGHT are solar power's prospects?

A business-as-usual approach will not work. Over time, economies and policies may spontaneously migrate to more efficient, more environmentally benign energy technologies, but those responses will almost certainly be too slow to stave off massive climate disruptions, which require that greenhouse gas emissions be capped within 50 years. This magazine has long taken the position that the best strategy will probably require calling on every available option: not only solar, wind, nuclear and other sources of power but also cleaner coal and more extensive conservation. Still, if only as an exercise in showing what might be possible, it is sometimes worth contemplating how much a single brace of related technologies can do.

In "A Solar Grand Plan," beginning on page 64, Ken Zweibel, James Mason and Vasilis Fthenakis sketch out how the U.S. could build a solar energy infrastructure that might provide two thirds of its electricity and one third of its total energy by 2050—enough to make the nation independent of overseas oil and to drop carbon dioxide emissions to a bit more than a third of what they are now. The authors do not invoke hypothetical breakthroughs in solar technologies; they rely on existing technology and incremental improvements to it. By their estimate the scheme would require $420 billion in subsidies over 40 years. But that sum could be a bargain in terms of energy and environmental security—as they point out, it is in line with other major expenditures, such as farm supports (and, we might point out, funding for the Iraq War). Whether their analyses are correct and whether such a solar plan is really the best choice available are open to debate, but that is rather the point: it behooves all of us to think boldly about what should be done and not to be intimidated by the problem's large scope.

Zhong Lin Wang describes a very different approach to obtaining and conserving energy in "Self-Powered Nanotech," starting on page 82. The systems of tiny piezoelectric elements he and his colleagues are developing could be ideal for powering microscale devices. They can tap into the ambient energy in their surroundings—for instance, future medical appliances might draw power from the rush of blood through veins. Expect such self-powered systems to play a pervasive role in tomorrow's technology. Wang's article is a good counterpoint to that of Zweibel, Mason and Fthenakis: to deal with our energy and environmental challenges, we can't be afraid to think big, but we also should not overlook the small. ■

JOHN RENNIE
editor in chief

FLYNN LARSEN (*Rennie*); MIKE ROESSLER *Corbis* (*solar panels*)

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directs the Center for Nanostructure Characterization at the Georgia Institute of Technology and has received multiple awards for his accomplishments in constructing nanoscale devices.

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Obesity ▪ Weight and Mortality ▪ Caloric Beverages

SEPTEMBER 2007

"Our 2005 paper on the excess mortality associated with levels of BMI in the U.S. did not state or imply that excess fat carries no health risks."
—Katherine M. Flegal et al.

Feast and Famine

The special issue on obesity ["Feast and Famine"] did not adequately address the skepticism that has developed concerning health research. Too often we have been encouraged to, say, increase our consumption of broccoli or oatmeal, only to then be told that the initial claims were faulty or exaggerated. These inconsistencies often arise from the misapplication of the basic principles of scientific methodology. There is a chronic failure to select unbiased samples, to identify appropriate control groups, to employ reliable statistical techniques and to recognize that correlation does not necessarily imply cause.

Christopher Bruce
Calgary, Alberta

I am a little surprised that you permitted the use of such a fuzzy measurement as body mass index (BMI). Like a number of other people at my gym, I am well into the "overweight" zone, not because of fat but because once a person carries a substantial amount of muscle, that person rates as overweight on a BMI scale. BMI is not only widely used in both popular works and professional analyses but is cited in public policy making, which makes the notion that it applies to only some part of the population a bit dreadful.

David Seaver
via e-mail

I was disappointed that your solutions for obesity and overeating explored pharmacological interventions and food choices and ignored the interrelation between emotions and food. All addictions, including food obsessions, have the same roots: low self-esteem, a feeling of an inexplicable void, the inability to process emotions or responses to stress, and a sense of being out of control, which manifests as a variety of self-destructive and compulsive tendencies.

Jennifer Delaney
via e-mail

The Consequences of Corpulence

Paul Raeburn should have consulted us before addressing our 2005 paper on the excess mortality associated with levels of BMI in the U.S. in "Can Fat Be Fit?" We did not state or imply that excess fat carries no health risks. On the contrary, we found that death from all causes was more likely among the obese (BMI 30 and over) than among those of normal weight.

We found no excess mortality among the overweight (BMI between 25 and 30)—a finding that has been reported by other large prospective studies such as the Seven Countries Study and the Cardiovascular Health Study. Our study carefully controlled for smoking and other possible confounding factors. Nevertheless, we checked whether the results could have been affected by smoking or preexisting

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Read an expanded version of the letter by Flegal et al. at
www.SciAm.com/ontheweb

ANSWERS to the December 2007 crossword.

illnesses by running numerous additional analyses. These analyses, published online by the *American Journal of Epidemiology* in August 2007 and on the Centers for Disease Control and Prevention Web site, found no confounding in our results.

It is important to remember that nutritional reserves may offer a survival advantage in some illnesses. That may be particularly true for the elderly, among whom most deaths occur.

Katherine M. Flegal
David F. Williamson
Centers for Disease Control and Prevention

Barry I. Graubard
Mitchell H. Gail
National Cancer Institute

Soup Is Good Filling?

In "The World Is Fat," Barry M. Popkin states that humans did not evolve to become satiated by beverages because water lacks calories. Calories in drinks such as soda contribute to obesity, he explains, because people tend to consume them in conjunction with more calories from food. But many people lose weight by going on soup diets, and he notes that we did evolve to consume breast milk (a breast-feeding baby will get full). Why is it that soup and breast milk can satiate humans if beverages cannot?

Forest Ray
New York City

POPKIN REPLIES: *Many studies have shown that soup does make us feel full, whereas caloric and noncaloric beverages do not. We are unsure if this appetite satisfaction is because of the salt or fat in soup, the way it is consumed, our perception of it as a filling food, or other reasons. Similarly, many studies have demonstrated that beverages containing sugar, high-fructose corn syrup or alcohol are handled differently by the body than when sugar or high-fructose corn syrup is incorporated in solid foods; as a result, the overall caloric intake from solid food does not adjust to account for the calories in these beverages. The mechanism responsible for that weaker compensatory response to fluids is unknown. I posited the hypothesis that humans may lack a physiological basis for processing carbohydrate or alcoholic calories in beverages because only breast milk and water were available for the majority of our evolutionary history. Another possibility is that carbohydrate- and alcohol-containing beverages may produce an incomplete satiation sequence that prevents us from becoming satiated on them. George Bray of Louisiana State University, my co-author for a study that will amplify these theories, suggests that one possible mechanism is the way the gastrointestinal tract responds to the form in which it is exposed to nutrients.*

ERRATUM "Developmental Disorder in Mice Reversed," by Nikhil Swaminathan [News Scan], incorrectly states that Fragile X syndrome causes cognitive dissonance. The text should have read "cognitive deficits."

CLARIFICATION The box "A Champion for Biotech," by Graham P. Collins, on page 108, should have clarified that research at the University of Cape Town in South Africa into developing maize genetically modified to be resistant to the maize streak virus is a joint effort between Edward P. Rybicki's group (Dionne N. Shepherd in particular) and Jennifer Thomson's.

Letters to the Editor

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

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Uncertainty ▪ Limited Flight ▪ Forbidden Territory

Compiled by Daniel C. Schlenoff

JANUARY 1958

UNCERTAINTY—"It may seem a paradox that one of the cornerstones of modern physics is something called the principle of uncertainty. The idea of indeterminacy as a rule of science does, in fact, disturb many 20th-century philosophers. But the uncertainty principle has proved a powerful answer—so far the most fruitful—to important questions in present-day physics. During the past decade the validity of the uncertainty principle has been argued voluminously, both by writers who understand the problems at issue and by writers who do not. Up to the present this so-called 'Copenhagen interpretation of the quantum theory' has stood its ground. In my opinion and in the opinion of many other theoretical physicists, the uncertainty principle will stand its ground indefinitely. —George Gamow"

KRILL—"The whale's example shows that we can reap vastly increased returns from the biological economy of the oceans. The 270 million tons of krill on which the Antarctic whales fed in their heyday would be more than enough to supply the annual requirements of the entire U.S. population. There are growing indications that krill may be a timely subject. Some 250 ships and 16,000 men—the largest whaling fleet in history—are now operating in the Antarctic Ocean. They depend mainly on the fin whale. If and when this species follows the blue and humpback whales into near-extinction, whalers may find it worthwhile to turn their attention to krill."

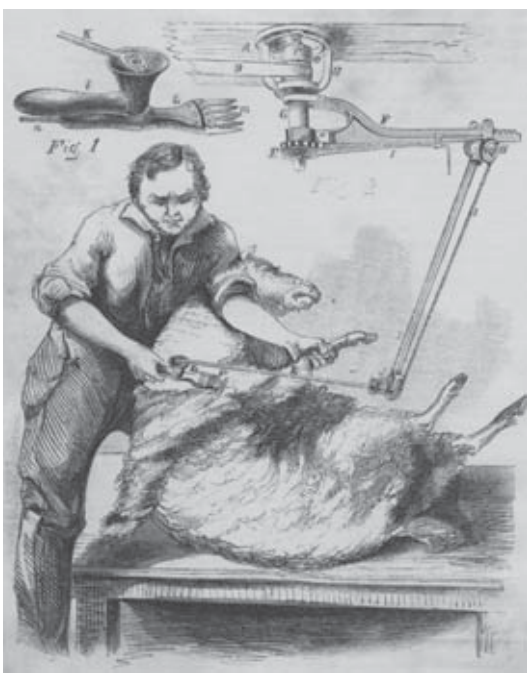
JANUARY 1908

FARMAN'S FLIGHT—"M. Henri Farman, on Monday, January 13, before the officials of the Aero Club of France, won the Deutsch-Archdeacon prize of 50,000 francs for the first flight by a heavier-than-air machine of one kilometer in a closed circuit. By Farman's recent successful flight in a circle, the record of the Wright brothers made in this country over two years ago has in this respect been duplicated; however, Farman has found that his machine in its present condition is incapable of long-distance flight, because of its inability to lift any perceptible quantity of fuel. Also, he has not demonstrated its capability of flying with safety against a wind having a velocity of 20 miles an hour—a feat which the Wright brothers accomplished with their first motor-driven machine in 1903."

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

JANUARY 1858

SHAGGY SHEEP—"One of the oldest materials used in the manufacture of fabric is the wool and hair of animals. The scissors or shears used for this purpose were very primitive indeed, being only two blades and a spring back; and with this simple implement sheep have been sheared for thousands of years past; it is but lately that a new implement has been introduced which can be worked by power, thus leaving the operator all his strength to manage the sheep and guide the shears. Our engraving represents a sheep being sheared by one of these machines, which is suspended from a beam."



SHEAR POWER: Mechanizing agriculture, 1858

NIGHT INTO DAY—"Whale oils are in comparatively limited use for illumination, and are becoming more limited every year. Sperm oil has no superior among all the burning fluids, but it has become so dear that cheaper substitutes have been sought and obtained. The most common of these is a compound of alcohol and turpentine, commonly known by the name of burning fluid, which is very cheap and cleanly. This fluid was first brought into public use in 1830. Were it not so volatile, no burning fluid could be more desirable. Horrible accidents, causing death in many instances, have occurred from the explosion of lamps, hence a safer substitute is desirable."

BLACK HILLS—"The St. Louis (Mo.) *Republican* states that a party has just recently returned to that city from an exploring expedition in a wild region known as The Black Hills. It is a vast country of movable sands, sterile, bleak and inhospitable. There are small streams at remote distances in it, upon which there is spare vegetation; sufficient, however, for the subsistence of the Indians' horses and some buffalo. The party consisted of sixty men, and the Sioux, who are numerous there, forbid the return of any more white men. They said that this party might pass, because it was the first, but no others may come, as they scared away their game, and would discover their strongholds and hiding-places."

SCIENTIFIC AMERICAN, VOL. XIII, NO. 17, JANUARY 2, 1858

Dimmed Hopes ▪ Vioxx Settlement ▪ Prion Holes ▪ Nukes and No Nukes

Edited by Philip Yam

Vioxx Payout

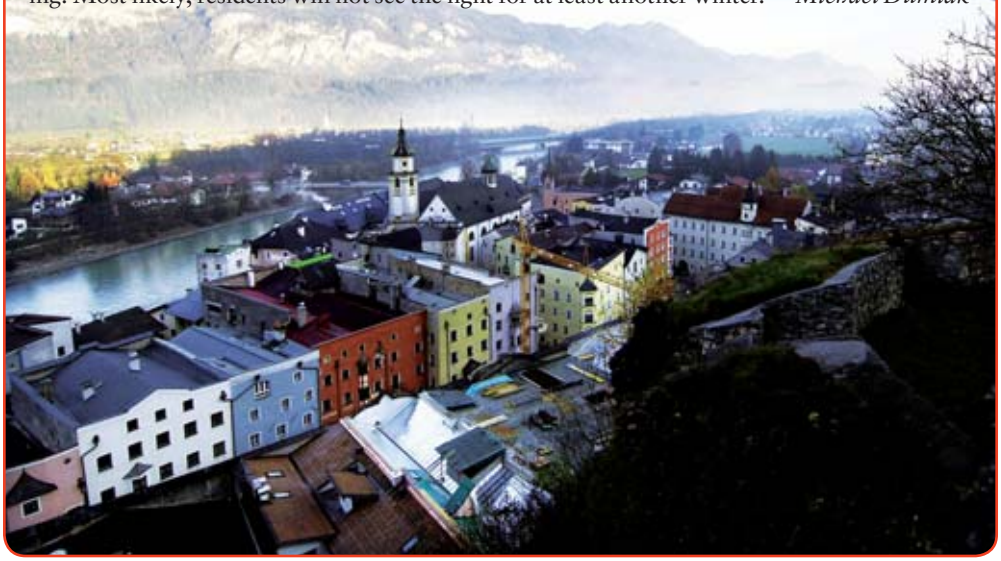
Merck appears to have closed the chapter on Vioxx, as the pharmaceutical giant agreed to pay $4.85 billion to plaintiffs. Clinical trials had revealed that the painkiller raised the risk of heart attack and stroke [see "Avoiding Another Vioxx"; SciAm, February 2005]. But Merck won most of the trials to reach juries, because plaintiffs' lawyers had a hard time linking any particular problem with the drug itself. The settlement, which represents a bit less than Merck's expected 2007 earnings, is much smaller than the $25 billion some analysts had expected Merck would have to pay.

Prion Disease without Prions?

Abnormal proteins known as prions play an essential role in the development of brain-destroying diseases that affect cows, deer and humans, among other mammals. Tests for these illnesses look for an enzyme-resistant form of the prion [see "Shoot This Deer"; SciAm, June 2003, and "Detecting Mad Cow Disease"; SciAm, July 2004]. But looking for that version may miss some cases. In a study published online October 8 by the *Journal of Biological Chemistry,* researchers found that mice that died of a "mad cow" infection failed to show any of the enzyme-resistant, misfolded prions. The results hint that other states of the prion may be the cause of infection or that prions are a by-product of an infection triggered by some other, as yet unidentified pathogen.

Here Doesn't Come the Sun

A town that gets no sun sounds like Gothic horror, but that is the case in winter for Rattenberg, an Austrian village nestled among huge mountains. Two years ago the residents hoped by now to have installed 15 large mirrors, or heliostats, which would reflect the sun's rays onto streets [see "Lifting the Winter Dark"; SciAm, April 2006]. Budget problems, however, have dimmed Rattenberg's hopes. The town had lined up Bartenbach Light Laboratory—an innovator in lighting design—and Bomin Solar, and the European Union kicked in money. But additional funding sources fell through, and Bomin dropped out. Bartenbach research director Wilfried Pohl says the lab recently met with town officials to find alternative financing. Most likely, residents will not see the light for at least another winter. *—Michael Dumiak*



The Not New Thing

Physicist Sidney Drell and former secretaries of state Henry Kissinger and George P. Shultz have all endorsed a "world free of nuclear weapons" and urged governments to work "energetically on the actions required to achieve that goal" [see "A Need for New Warheads?"; SciAm, November 2007]. In a recent letter to senators, however, they wrote that development of the Reliable Replacement Warhead (RRW) "should certainly go ahead."

The two points evidently do not contradict each other. "I never said kill RRW," Drell says. In the course of changing the world to what we want it to be, "we have to maintain the [nuclear warhead] stockpile as safe and reliable." The stockpile includes the warheads (*above*) on the MX missile.

Drell's endorsement rests on several assumptions, he notes: that RRW is not a weapon for new applications, that it does not drain funds from the successful maintenance of existing weapons and that it would not violate nonproliferation treaties. Although experts wonder whether the RRW can be certified as reliable without testing, Drell insists that "no new testing is absolutely critical" to help ensure U.S. integrity concerning test bans and nonproliferation. *—David Biello*

DAVID KADLUBOWSKI *Corbis (Vioxx);* NUKEPHOTO.COM/PAUL SHAMBROOM/AURORA PHOTOS *(MX warheads);* ROBERT PARIGGER *AP Photo (Rattenberg)*

MEDICINE

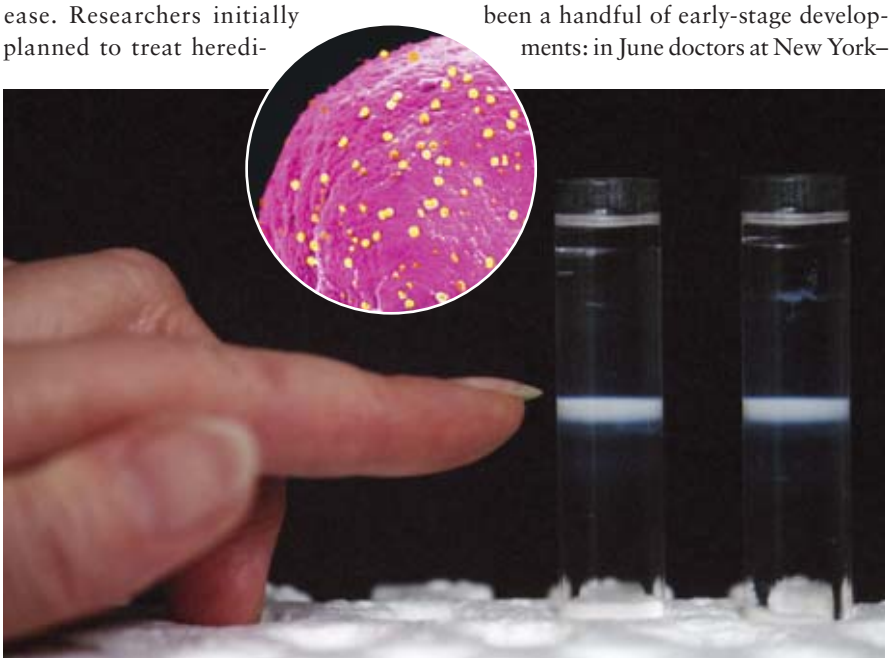
Regaining Lost Luster

New developments and clinical trials breathe life back into gene therapy BY MELINDA WENNER

The past 15 years have been a roller coaster for gene therapy. After being touted in the early 1990s as "the medicine of the future," gene therapy left an 18-year-old dead and three others with leukemia; in July it was tied to the death of a 36-year-old Illinois woman undergoing treatment for rheumatoid arthritis, although further investigation cleared her therapy of the blame. Gene therapy scientists, however, believe they can put the bad news behind them, thanks to a handful of recent developments and others just over the horizon.

Gene therapy describes any treatment in which doctors insert new or modified genes into a person's cells to treat or prevent disease. Researchers initially planned to treat hereditary disorders such as cystic fibrosis, in which normal gene products are deficient, by delivering functional copies of missing genes to cells that need them. Since then, scientists have expanded gene therapy's possible applications to include "training" immune cells to hunt down cancer, building new blood vessels and making the immune system resistant to infection.

"We really don't know the full dimension of what it can do," says Arthur Nienhuis, a hematologist at St. Jude Children's Research Hospital in Memphis and president of the American Society of Gene Therapy (ASGT). In addition to 12 cancer treatments and a heart treatment currently in large phase III clinical trials, there have been a handful of early-stage developments: in June doctors at New York–Presbyterian Hospital announced promising results from a phase I trial for Parkinson's disease; a therapy that has restored sight to 70 congenitally blind dogs is being tested in humans at the University of Pennsylvania; and eight research groups are gearing up to test new HIV treatments. Although no gene therapies have yet been approved by the U.S. Food and Drug Administration, more than 800 trials are ongoing; China has approved two cancer treatments, but their efficacy remains unclear.



SPECIAL DELIVERY: Viruses carrying human genes accumulate in the blue layer of liquid after centrifugation. So modified, the virus can deliver its payload to treat or prevent diseases. The inset shows ordinary adenoviruses (*yellow*) on a red blood cell.

CNRI *Photo Researchers, Inc.* (*scanning electron micrograph*); PHILIPPE ERANIAN *Corbis* (*test tubes*)

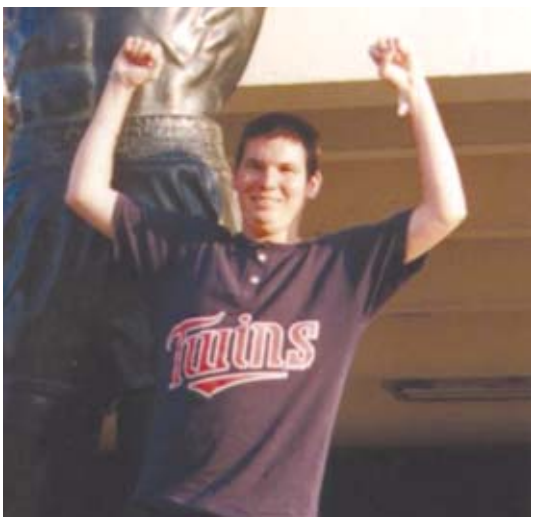
What makes gene therapy so promising also makes it extremely challenging. It can target only those tissues that need it, "which is a major contrast with traditional pharmacotherapy, where you take a pill or receive an injection, and a very, very small portion of the injected or ingested drug actually arrives at the [correct] site," says David Dichek, a cardiologist at the University of Washington. But ensuring that the gene reaches its target is no small feat. Trials can skirt this problem when targeted cells can be injected directly or easily removed—with the latter method, doctors can manipulate isolated cells in the lab and replace them in the patient later. But getting genes to inaccessible targets has been one of the field's biggest hurdles.

Most scientists use modified viruses as "vectors" to deliver gene therapy. Viruses are good at delivering genetic payloads to cells; after all, that is what they do. If scientists strip viruses of their genetic material and replace it with therapeutic genes, viruses will deliver this payload to the cells instead. Different viruses do different things—some attack the liver, others nerves; some insert their DNA into the host genome, others do not—so physicians

can choose those that best suit their purposes and further engineer them if need be. "There's been a lot of effort to steer viruses to go specific places," says Donald Kohn, an immunologist at the Keck School of Medicine of the University of Southern California and Childrens Hospital Los Angeles.

But viruses come with a catch: "Our immune system developed to reject them," Kohn explains. What killed 18-year-old Jesse Gelsinger in 1999 was a powerful immune response to his therapy, not the therapy itself. So even if a vector reaches its target, scientists must ensure that the body does not attack the "infected" cells. Recently scientists have identified a number of ways of achieving this, by using lower therapy doses, pretreating patients with immunosuppressive drugs and masking vectors so immune cells do not notice them. Some scientists also use vectorless "naked" DNA and genes packaged in other ways.

Even if gene therapy conquers these challenges, will it ever overcome its negative reputation? Some scientists maintain that it has never been that unsafe, relatively speaking. "If you compare the safety profile of gene drugs in development versus the traditional small-molecule pharmaceutical drugs, there's no evidence that gene therapy is any more dangerous," says Savio Woo, an oncologist at Mount Sinai Hospital in New York City. Thousands of patients have been treated, and only a few adverse events have been reported, he states; the leukemia that developed in three "bubble boy" patients may have been a side effect specific to the therapeutic gene, which stimulates immune cell growth. "Any time a few cells divide a lot, you always worry about secondary genetic changes, which is how cancers form," notes Mark Kay, a geneticist at Stanford University.



TRIALS AND TRIBULATIONS: The death of Jesse Gelsinger during a gene therapy trial in 1999 gave the field a shock from which it is slowly recovering.

MBR Newscom

As the field continues to evolve and improve, scientists hope that the public's perceptions of it will, too. "We clearly have had clinical successes, and now we're on the threshold of achieving many more," says ASGT president Nienhuis. "I think we're going to hear a lot about them in the next several years."

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

FOOD SCIENCE

A Dash of Nutrition

Iron- and vitamin-fortified salt gets set to fight deficiency diseases BY DIANE MARTINDALE

The fortification of salt with iodine is a global success story: with two out of three households in the developing world now consuming iodized salt, an estimated 82 million children are protected from thyroid disease and resultant learning disabilities every year. Still, people suffer from a lack of other micronutrients.

For years, food scientists have looked for a way to fortify iodized salt to combat iron-deficiency anemia, which affects some two billion people, as well as vitamin A deficiency, which afflicts at least 100 million children in poor countries and is the leading cause of blindness among them. Canadian researchers have now developed a practical way to double- and triple-fortify salt, which might also be more acceptable to people than genetically modified foods in tackling malnutrition.

Adding iron to iodized salt is a simple idea that has proved difficult to execute. The chemicals are incompatible: when mixed together, iodine vaporizes and iron degrades. After more than a decade, Levente Diosady, a chemical engineer at the University of Toronto, finally solved the problem by borrowing a technique from the food industry referred to as microen-

Nourishing Soft Drinks?

Besides fortifying salt, Levente Diosady of the University of Toronto has also developed a method to purify rapeseed protein, a by-product of canola oil manufacture. "The protein meal is highly nutritious, but it comes out as black sludge," Diosady explains. His process separates the protein from bitter compounds and then concentrates it into a neutral-tasting powder that contains all the essential amino acids. Similar to soy, the canola protein has the additional quality of being soluble in acidic liquids and hence could supplement soft drinks, which in developing countries are often consumed in lieu of water because of safety concerns. Diosady plans to develop a protein-enriched soft drink called LiveADE.

capsulation. The process involves spraying iron particles with stearine, a vegetable fat, which creates a protective coat and prevents the iron from reacting with the iodine.

Encapsulating the iron, however, was only part of the solution. Diosady's team also had to change the appearance of the iron particles—which are dark brown and much smaller than salt grains. "The iron can't look like mice droppings in the salt," Diosady says. "This is important in developing countries where food contamination is a problem."

So to make the iron resemble salt, Diosady first sprays the microscopic iron granules with maltodextrin, a modified food starch that acts like a glue to bind the iron particles together until they form spheres about the size of salt crystals. He then spray-coats the iron clusters with hot vegetable fat containing food-grade titanium dioxide, a whitening pigment. When mixed with iodized salt, the modified iron capsules are nearly imperceptible. Vitamin A can also be added using a similar method to create triple-fortified salt.

Field tests in Nigeria and Kenya showed that the double- and triple-fortified salts are stable in humid and hot climates and acceptable to the locals. The Micronutrient Initiative, an Ottawa-based nongovernmental organization, tested iron-enriched salt in Ghana, where in eight months the number of anemic children dropped by 23 percent without any other iron supplementation. The technology has been scaled up in two large plants in India, and the initiative is currently leading a study with 3.6 million schoolchildren.

Salt is an ideal vehicle for providing micronutrients, Diosady notes, because almost everyone consumes it and it is relatively inexpensive to fortify—about 1.7 cents per kilogram of salt for double-fortified salt. "Even the poorest of the poor have to barter or buy salt. There's no person in the world so poor that they have to make their own salt," he says. Also, the amount of salt eaten in a given population is about the same, making dosage easier to control. People might also accept fortified salt more readily than genetically modified foods such as Golden Rice, which contains beta-carotene, a precursor to vitamin A. The rice has yet to be introduced into developing countries amid fears about its safety and concerns that the crops may not have high enough concentrations of micronutrients.

But fortified salt cannot supply all the critical nutrients. For instance, vitamin C is needed in such large quantities that it would end up carrying the salt, not the other way around. And because, on average, the daily intake of salt is 10 grams, the fortified version could only supplement a person's nutritional requirements, not supply all of them.

Howarth Bouis, director of HarvestPlus, an international research program that seeks to reduce micronutrient malnutrition with enriched staple foods, believes that fortifying commercial products such as salt can work in urban regions, but such efforts may not be able to reach all those in need, especially the poor living in remote rural areas. Instead HarvestPlus promotes the use of biofortified crops, produced through either conventional plant breeding or genetic modification. With this strategy, Bouis says, people can grow for themselves the nutrient-rich foods that they need: "It is the plants that are doing the work and not manufacturers." But the process of biofortification can cause color changes to the foods, so convincing consumers to accept them could be a challenge.

Everyone agrees that a balanced diet is the best way to combat micronutrient deficiencies. But for people in the developing world without access to such a diet, they might take their nourishment with a few grains of fortified salt.

Diane Martindale is a science writer based in Toronto.

NOW WITH IRON: A key to making fortified salt acceptable to people is to ensure that the iron looks like salt. In the vials (*clockwise from top left*): iron particles; iron coated with titanium dioxide; iodized salt; and iodized salt mixed with the coated iron.

ANDREW DIOSADY *University of Toronto*

ASTRONOMY

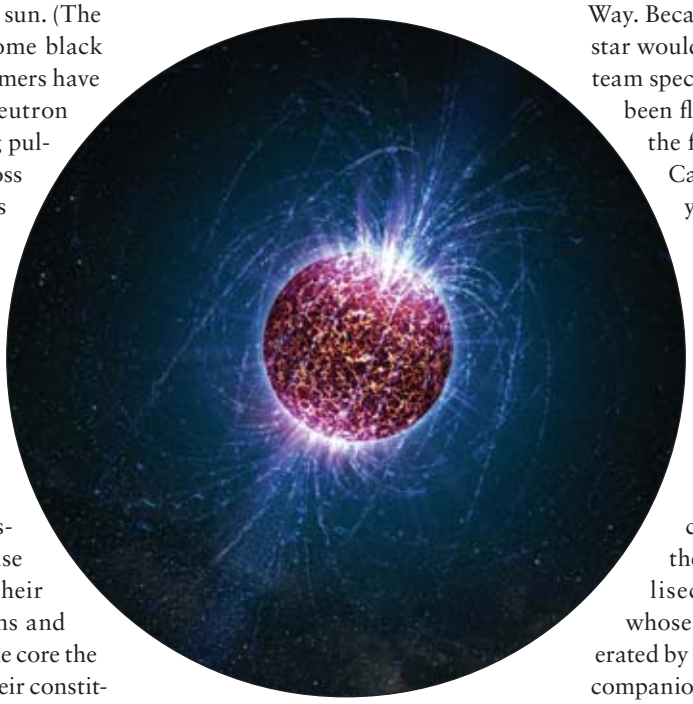
Neutron Oddball

A newly discovered neutron star doesn't behave like it's supposed to BY MARK ALPERT

Our galaxy is littered with the corpses of dead stars. At the end of their useful lives, the vast majority of the stars in the Milky Way shed their outer layers and shrink to white dwarfs, dense spheres about the size of Earth. But very massive stars explode in supernovae and leave behind even denser relics, called neutron stars, which are only 20 to 40 kilometers across but weigh more than our sun. (The most massive stars of all become black holes.) Since the 1960s astronomers have observed a wide variety of neutron stars, including madly rotating pulsars that sweep radio beams across the galaxy and x-ray binaries that devour material pulled from their companion stars. But last August researchers announced the discovery of perhaps the oddest neutron star yet, a lone x-ray emitter in the Ursa Minor constellation that does not seem to fit into any observed category.

Scientists have long been fascinated by neutron stars because their physics is so extreme. Their crushing gravity fuses electrons and protons into neutrons, and at the core the neutrons may break down to their constituent quarks. To better understand the formation and evolution of these bodies, some researchers have focused on isolated neutron stars (INS) that have moved away from the nebulous remnants of the supernovae that created them. Over the past decade astronomers have detected seven such objects that emitted x-rays observed by the German space telescope ROSAT but produced no radio beams like the ones generated by the rotation-powered pulsars. Dubbed "The Magnificent Seven" after the classic 1960 movie, the neutron stars were deemed to be relatively nearby (most of them less than 2,000 light-years from the sun) and relatively young (probably less than a million years old).

In an effort to find additional INS objects, a team composed of Robert Rutledge of McGill University and Derek Fox and Andrew Shevchuk, both at Pennsylvania State University, identified another ROSAT x-ray source in a patch of sky where there were no ordinary stars. Closer observations with space- and ground-based telescopes revealed an object whose spectrum was roughly similar to those of the Magnificent Seven. But the new object was different enough from the other INS sources that the researchers eventually named it Calvera, after the villain who fought the seven hired gunmen in the film. Calvera is located at an unusually high galactic latitude; from Earth's perspective, the neutron star is about 30 degrees above the disk of the Milky Way. If one assumes that Calvera has the same characteristics as the other INS objects, then the neutron star must lie 25,000 light-years from Earth and 15,000 light-years above the galactic plane.



ON ITS OWN: Artist's rendition of an isolated neutron star shows the magnetic field lines surrounding the ultradense stellar remnant.

CASEY REED *Courtesy of Pennsylvania State University*

That position would put Calvera squarely in the galactic halo, the diffuse spherical region surrounding the Milky Way. Because it is unlikely that a neutron star would form in the halo, the research team speculated that Calvera might have been flung out of the galactic disk by the force of its violent birth. But if Calvera formed less than a million years ago, as the models predict, it would have had to fly out of the Milky Way at a blistering speed of more than 5,000 kilometers per second, which is far faster than any other neutron star.

This conundrum led the researchers to reconsider Calvera's classification in the INS category. They postulated that the object might instead be a millisecond pulsar, a neutron star whose rotation has been wildly accelerated by the accretion of material from a companion star (which, in Calvera's case, would have been fully devoured or dispersed long ago). If this hypothesis were true, Calvera would be a lot closer to Earth: between 250 and 1,000 light-years away, making it one of the nearest neutron stars. But when the investigators pointed a radio telescope at Calvera, they did not detect the ultrafast pulses expected of a millisecond pulsar. "That definitely deepened the mystery," Fox says. The researchers are planning more observations of Calvera to clarify its status. And in the meantime, they are beginning to study 10 other isolated x-ray sources that may turn out to be equally baffling.

EVOLUTION

Paging Dr. Doolittle

The "language" gene *FOXP2* proves critical for animal vocalizations BY JOHN WHITFIELD

"Nothing shows that Neandertals *didn't* have language abilities," says Johannes Krause of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Indeed, the recent finding by Krause and his colleagues that Neandertals and humans have the same version of the gene *FOXP2*—the only gene linked to language so far—might be thought of as evidence that they did.

But although studies of modern humans suggest that *FOXP2* is necessary for speech, no one believes that it is sufficient. The gene is "just one piece of a complicated puzzle," says geneticist Simon Fisher of the University of Oxford, part of the team that discovered it. As such, the Neandertal sequence is interesting but provides little information about their linguistic skills. "No single genetic factor can tell us whether or not an extinct species was capable of speech," Fisher says.

Despite several years of intense study, researchers are still unsure what *FOXP2* does or how it might have contributed to the evolution of language. Studies of extinct humans have yet to uncover much about these things, but studies of living animals are starting to provide some hints. The gene has been implicated in many of the most sophisticated sounds in the animal kingdom, suggesting that these behaviors are the foundation on which human language is built.

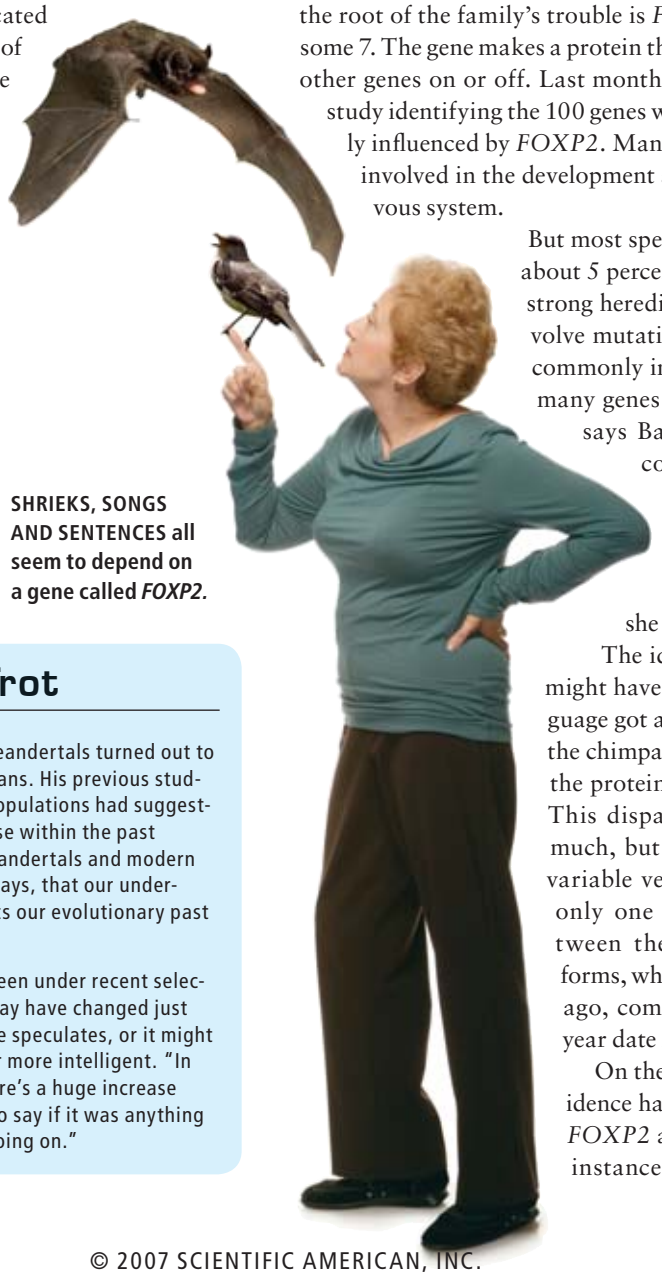
An English family known as "KE" revealed the link between *FOXP2* and language. Many members of this family have severe difficulties with language. They struggle to control their facial movements and have difficulty with reading, writing, grammar and understanding others.

In 2001 Fisher and his colleagues found that the gene at the root of the family's trouble is *FOXP2*, located on chromosome 7. The gene makes a protein that binds to DNA, switching other genes on or off. Last month Fisher's group published a study identifying the 100 genes whose activity is most strongly influenced by *FOXP2*. Many of the genes turn out to be involved in the development and organization of the nervous system.

But most speech disorders—which affect about 5 percent of all children and have a strong hereditary component—do not involve mutations in *FOXP2*. They more commonly involve interactions between many genes and environmental factors, says Barbara Lewis, who studies communication disorders at Case Western Reserve University. "It's a very important gene, but it's not the only speech gene out there," she says.

The idea that changes in *FOXP2* might have driven the evolution of language got a boost from the finding that the chimpanzee and human versions of the protein differ by two amino acids. This disparity might not sound like much, but *FOXP2* is one of the least variable vertebrate proteins. There is only one amino acid difference between the mouse and chimpanzee forms, which diverged 60 million years ago, compared with the six-million-year date for the human-chimp split.

On the other hand, more recent evidence has muddied the link between *FOXP2* and language evolution. For instance, the mutations that cause



SHRIEKS, SONGS AND SENTENCES all seem to depend on a gene called *FOXP2*.

PAUL BURNS *Getty Images (woman)*; ALTRENDO NATURE/GETTY IMAGES *(bird)*; MICHAEL DURHAM *Minden Pictures (bat)*

Doing the *FOXP2* Trot

Johannes Krause was surprised when Neandertals turned out to have the same version of *FOXP2* as humans. His previous studies of the genetic variation in modern populations had suggested that the human form of the gene arose within the past 200,000 years—150,000 years after Neandertals and modern human lineages diverged. It shows, he says, that our understanding of how current genetics reflects our evolutionary past may need revising.

But Krause still thinks that *FOXP2* has been under recent selection pressure in the human lineage. It may have changed just before Neandertals and humans split, he speculates, or it might have helped make our common ancestor more intelligent. "In the fossil record 500,000 years ago, there's a huge increase in brain size," Krause notes. "It's hard to say if it was anything to do with *FOXP2*, but something was going on."

speech defects in humans do not affect those parts of *FOXP2* unique to us. And "some of the changes in humans previously thought unique are seen in other mammals," such as cats, says Stephen Rossiter of Queen Mary, University of London. "As we're looking at more species, we're seeing more differences. The picture is getting complicated."

In September, Rossiter and his colleagues revealed that bats, which use echolocation are an exception to the rule of *FOXP2*'s unchanging nature: the gene varies widely within the group. "There's double the number of changes within bats as compared with all the other vertebrates surveyed," he says. The finding supports the idea that human *FOXP2* is particularly important in the physical control of speech. Like talking, which engages more than 100 muscles, making the sounds needed for sonar requires "massively complex coordination of the face and mouth," Rossiter says.

Bats are one of the few animals that show vocal learning, along with humans, some songbirds, whales and dolphins. That is, the sounds they make are not innate but require practice and imitation. Studies in songbirds support the link between *FOXP2* and vocal learning, suggesting that as well as controlling how our brain forms, the gene might also influence how we use it. The gene changes its activity in the brains of adult birds when they learn and practice their songs, neuroscientist Stephanie White of the University of California, Los Angeles, has found. "Birds may have the same circuitry that formed the foundations for human language," White explains. The evidence points to *FOXP2* being a switch, she says, that different species put to varying uses in their neural machinery.

The gene's story hints at how evolution puts old materials to new uses, points out psychologist Gary Marcus of New York University. "It's a very good entrée into language and how it relates to whatever preadaptations for language we inherited from our ancestors."

John Whitfield is a freelance science writer based in London.

PHYSICS

Making Space for Time

Physicists meet to puzzle out why time flows one way BY SCOTT DODD

FREDRIK SKOLD *Getty Images*

"Emoclew dna olleh," Columbia University string theorist Brian Greene said as he opened a conference at the New York Academy of Sciences last October. "If you understood that as 'Hello and welcome' in time reverse," he clarified, "you probably don't need to be here."

No one left. Many of the world's top theoretical physicists and cosmologists gathered at the conference to grapple with the mystery of how time works. New telescope observations and novel thinking about quantum gravity have convinced them that it is time to reexamine time. "We've answered classic questions about time by replacing them with other hard questions," says cosmologist Max Tegmark of the Massachusetts Institute of Technology.

On the face of it, time seems pretty simple, like a one-way street: eggs don't unscramble, laugh lines don't vanish (not without Botox, anyway), and your grandparents will never be younger than you. But the universe's basic laws appear to be time-symmetrical, meaning they are unaffected by the direction of time. From the point of view of physics, the past, present and future exist simultaneously.

For more than a century, physicists have proposed any number of explanations for this apparent contradiction, from the psychological (the flow of time is an illusion) to the physical (some unknown property of quantum mechanics reconciles the contradiction). None has proved satisfactory. In 1927 astrophysicist Sir Arthur Eddington coined the term "time's arrow" for the phenomenon and linked it to entropy: as the universe gets older, it becomes more disordered, following the second law of thermodynamics.

But scientists cannot explain why order lies in the past and disorder in the future. A solution has appeared so elusive that at times it has been regarded as a distraction from more "respectable" research. Physicist Richard Feynman even refused to have comments about time's arrow attributed to him at a conference in 1963, insisting on being identified as "Mr. X."

"The problem is at the borderline between science and philosophy, and a lot of people don't feel comfortable in that area," says Laura Mersini-Houghton, a physicist at the University of North Carolina at Chapel Hill and co-organizer of the conference. "It's been very difficult to make progress over the past 20 years, because there hasn't been much new to say."

That is all changing thanks to stronger instruments for probing the heavens. The cosmic microwave background radiation,

a remnant of the big bang, shows that 380,000 years after its birth, the universe was filled with hot gas, all evenly distributed and highly ordered. Eventually the early cosmos underwent inflation and began to coalesce into the disordered universe of stars and atoms we know today.

What remains puzzling, though, is why the early universe was so orderly—a condition that physicists consider highly improbable—and what caused it to swell so rapidly. "The arrow-of-time problem, once you get down to the nitty-gritty of it, is, Why was the early universe the way it was?" says Sean Carroll, a cosmologist at the California Institute of Technology. What is more, the cosmos is now going through another period of expansion, with galaxies flying apart at an increasing rate because of a mysterious dark energy. "The fact that it appears that the universe is just going to expand forever and get colder and colder makes [the different conditions] even more striking," Carroll adds.

Mersini-Houghton and her colleagues brought together some of the best minds in the field for the conference because, as she puts it, "we can't just brush this problem under the rug anymore and hope it will be solved by something else." Prominent physicists such as Greene, Tegmark, Lee Smolin of the Perimeter Institute for Theoretical Physics in Ontario, Paul Davies of Arizona State University and Andreas Albrecht of the University of California, Davis, invoked string theory, black hole equations and the idea that we live in one of many parallel universes as possible explanations.

The multiverse concept emerged as one of the more favored—or at least frequently talked about—theories for the strange tidiness of the early cosmos. "If you accept the idea that this might be only one of many possible universes, then that makes it more plausible," Mersini-Houghton says. Universes that started out more chaotic might not have survived or evolved to support intelligent life. So one-way time—and our entire existence, for

that matter—could be just a happenstance.

Several attendees said that understanding time is vital to helping them answer other fundamental questions, including what happens at the center of a singularity and whether cosmic inflation could one day reverse, causing the universe to collapse. And the growing cosmological data allow physicists to make predictions about the nature of time and the early universe that could soon be tested through new observations. "We can see a lot more than we could before, and that means we can be a bit more daring," Mersini-Houghton says. It's about time.

Scott Dodd is a freelance writer based in New York City.

ECOLOGY

Relative Distance

Hyena "wingmen" sacrifice sex for an unrelated male BY DAN EATHERLEY

In many animals, relatives tend to stay close, either sharing the same territory or living in neighboring ones. By sticking together, individuals can defend food, mates and other resources, thereby working to perpetuate the family genes, even if not all manage to breed or raise young.

One particular mammal, however, turns this general observation on its head, and experts in behavioral ecology do not quite understand why. Striped hyenas (*Hyaena hyaena*), which live in Africa and parts of Asia, demonstrate so-called protosocial tendencies. Although little direct interaction occurs among individual hyenas, a closer look reveals that they actually form spatial groups living on exclusive and stable ranges just like species that display obvious social behavior. One would expect relatives to share the same territory or to inhabit territories close together. This is not always so, however, claims Aaron P. Wagner, now at Michigan State University.

Wagner and his colleagues trapped an entire population of striped hyenas in Kenya's Laikipia District, about 135 miles north of Nairobi, and collected its members' DNA. The scientists also radio-tracked the animals to understand their movements. "As far as we are aware, the patterns of relatedness and space use we found in these hyenas are unseen in any other carnivore," says Wagner, who published some of the results of the four-year study in the October 2007 *Molecular Ecology*.

Wagner's team found that the spatial groups formed by this species always consist of just a single female defended by up to three males. Similar coalitions occur in other carnivores, but in those cases the males usually guard several females so that each male has a chance to mate. With only one female available, however, some male striped hyenas are unlikely to breed at all. Such sacrifice and cooperation could be understandable if all males were related, but genetic analysis showed that the hyena coalitions often include unrelated males.

A. P. WAGNER

RANGE ROVERS: Tracking collars revealed that, unlike other mammals that display social behavior, neighboring striped hyenas are often not related.

Even more remarkable, for both sexes, hyenas living in neighboring territories are less closely related than nonneighbors. Wagner found this arrangement puzzling because individuals that disperse and cross territorial boundaries are at great risk of being attacked and killed by others of their species. "Therefore, you would expect to find relatives living near one another and for relatedness to decline with distance," Wagner says.

No single theory can explain the overall patterns recorded. Wagner speculates that for males, any form of coalition—even with nonrelatives—might provide a temporary safe haven when the alternative of roaming alone is too hazardous or the chance of single-handedly defending a female is too low.

But given the dangers, why would striped hyenas leave their kin, risking death to travel to distant nonneighboring territories? Perhaps relatives settle in nonadjacent territories to avoid cross-border competition and costly fights with one another. In the spotted hyena (*Crocuta crocuta*), male and female group members sometimes engage in aggressive disputes with neighbors over food or mates—even battling with their own kin. Zoologist Kay E. Holekamp, also at Michigan State, questions the evidence that striped hyenas actually engage in these boundary conflicts at all and instead suggests that inbreeding avoidance might account for their odd patterns of dispersal. According to Wagner, however, the need to prevent inbreeding would not explain why low levels of relatedness were found among neighbors of the same sex.

Maybe, at the time of the study, there was nowhere else to go, suggests ecologist Hans Kruuk of the University of Aberdeen in Scotland. "Dispersing animals might not have found an empty space in a neighboring territory," meaning that individuals would have had to venture farther into several territories. Wagner doubts this saturated-environment scenario, arguing that it could explain why *some* relatives end up far away but does not explain why almost *none* ever live close by.

Calling the results "tantalizing," biologist Gus Mills of South Africa's Tony and Lisette Lewis Foundation, which funds nature conservation, appeals for longer-term studies. "Large carnivores are long-lived and reproduce quite slowly. Getting large samples over extended periods is very difficult and so is interpretation of results."

Wagner agrees and argues that research has been too skewed toward species with well-developed social behavior, such as lions or spotted hyenas. "Up to 90 percent of carnivores are, like striped hyenas, behaviorally solitary. We must learn more about the solitary majority before claiming we know why and how groups form and how sociality evolved."

Dan Eatherley is an environmental consultant and writer based near London.

PALEOANTHROPOLOGY

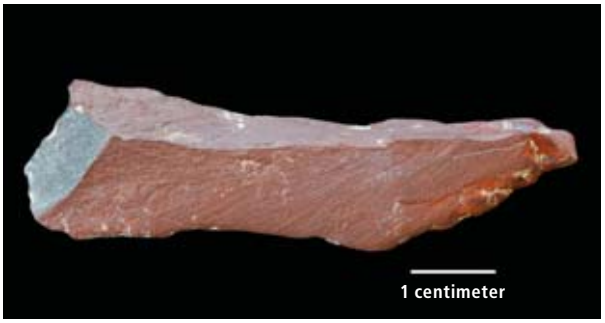
Food for Symbolic Thought

Besides the first seafood dinner, signs of the earliest symbolic thought BY JR MINKEL

A cave on the southern coast of South Africa contains a bowl's worth of edible shellfish dating back to about 165,000 years ago. Besides pushing back the earliest known seafood meal by 40,000 years, the discovery also marks the earliest time when people might have engaged in symbolic thought.

Anatomically modern humans probably emerged between 150,000 and 200,000 years ago in eastern Africa. When those humans first developed the potential for symbolic thought, including language, has remained a puzzle.

Looking for early human remains, Curtis W. Marean of the Institute of Human Origins at Arizona State University and his colleagues homed in on the caves at South Africa's Pinnacle Point. In addition to discovering the first known seafood dinner—mostly brown mussels—they found small stone blades and reddish rocks tossed in with the shells. They identified a dozen or so pieces of iron-rich hematite rock with flattened sides bearing parallel grooves, indicating that the shellfish eaters scraped the rocks to make powder. Mixing that powder with sap or another binder yields a reddish or pinkish paint, possibly to adorn the body or the face.



WHAT, NO LOBSTER FORK? Iron-rich blades of 165,000 years ago show grooves, suggesting that the shellfish eaters scraped them to obtain a red powder for painting.

That people were working with pigments back then "is a pretty good indicator of symbolic thought," says Marean, who published the findings in the October 18 *Nature*. A population living on shellfish would have stayed in one place and grown in number, he notes, increasing the need for negotiations between individuals or social groups, which might have led to a system of decorative markings.

COURTESY OF MOSSEL BAY ARCHAEOLOGY PROJECT

PESTICIDES

Bt-Beating Bugs

Researchers have long worried that crop-munching insects could become resistant to Bt, a toxin naturally produced by the microbe *Bacillus thuringiensis* that is harmless to most other organisms. Bt use is common; crops with the pesticide cover more than 32 million hectares of land worldwide—an area slightly larger than Italy. Mario Soberón of the National Autonomous University of Mexico and his colleagues investigated the most commonly used Bt toxins, which work by binding to specific receptors in pest midguts. They found three insect species that had evolved altered toxin receptors, which apparently grant Bt resistance. But the good news is that the researchers also constructed modified toxins that can kill Bt-resistant pink bollworms. These new toxins are slightly less potent than the original versions against vulnerable insects, but further research might improve them. Chew on the findings reported online November 1 by *Science*. —*Charles Q. Choi*

BOLLWORM munches on a cotton flower.

OBESITY

Weight Loss on Shaky Ground

Exercise takes energy, and presumably that is what combats obesity, but provocative experiments now suggest that jiggling might be enough. For 15 minutes almost every day for 15 weeks, scientists at Stony Brook University had mice sit on a buzzing platform that almost imperceptibly vibrated at 90 times per second, accelerating up and down at 20 percent the strength of the earth's gravitational pull. After this treatment, the mice had 27 percent less fat in their torso than mice kept on stationary platforms. They also had significantly reduced levels of fatty compounds linked with type 2 diabetes.

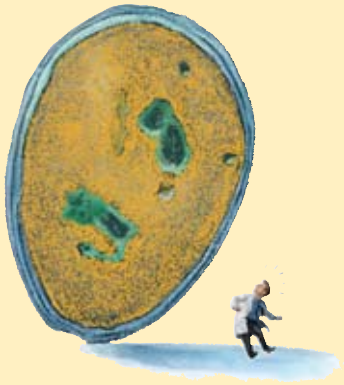
The researchers speculate that the vibrations inhibited the formation of fat cells from stem cells. The work could lead to a nonstrenuous, drug-free method for control of obesity, but the investigators caution that exercise remains key to weight control and loss. The results appear in the November 6 *Proceedings of the National Academy of Sciences USA*. —*Charles Q. Choi*

BIOLOGY

Bone Sweet Bone

Although sweets can help weaken teeth, sugars are apparently key to making bone strong. The extraordinary strength of bone depends on the complex, precise way in which its organic and inorganic components are ordered. Scientists had long thought that collagen and other proteins directly control the structure of bone. Now it turns out that sugary compounds are responsible instead—specifically, polysaccharides known as glycosaminoglycans and proteoglycans. Based on nuclear magnetic resonance imaging of horse bones, researchers conclude that polysaccharides help to guide the proper crystallization of bone minerals. Better understanding of how bone forms should alter the way osteoporosis and osteoarthritis are treated and perhaps lead to new ways of creating synthetic bone. This work may also strengthen the rationale for over-the-counter joint and bone pain remedies such as chondroitin, a glycosaminoglycan. Bone up on the research in the October 16 *Chemistry of Materials*. —*Charles Q. Choi*

Data Points



No Mercy from MRSA

New estimates of infections by an antibiotic-resistant bacterium, methicillin-resistant *Staphylococcus aureus* (MRSA), have astounded experts, who had not considered it a major public health threat. Researchers conducted population-based surveillance at nine sites and extrapolated the 2005 data for the entire U.S. Recent fatal cases of invasive MRSA in children have also raised some concerns, although most deaths happened to people older than 65, and infections tended to occur at hospitals, rather than at schools and playgrounds.

Number of MRSA cases in 2005:	8,987
Number of in-hospital deaths:	1,598
Estimated number of U.S. cases:	94,360
Estimated number of deaths:	18,650
Number of AIDS deaths in 2005:	17,011
MRSA infections per 100,000 people:	31.8
In those 65 years and older:	127.7
In those between five and 17 years:	1.4

SOURCES: Journal of the American Medical Association, *October 17, 2007; Centers for Disease Control and Prevention*

NIGEL CATTLIN *Holt Studios International/Photo Researchers, Inc. (bollworm)*; ILLUSTRATION BY MATT COLLINS

In Brief

FASTBALLS FROM BLACK HOLES

A network of 1,400 ground-based particle detectors and two dozen telescopes has located the possible origin of the highest-energy cosmic rays. Traveling at near light speed, these rays—most likely protons—pack 10^{20} electron volts, 100 million times the energy produced by the largest particle accelerators and roughly equivalent to that of a fast-pitch baseball. The source appears to be nearby active galactic nuclei: bright galactic cores probably powered by supermassive black holes. Scientists say they would never have guessed that black holes might have such powers if not for high-energy cosmic rays. *—JR Minkel*

MOTHER'S MILK AND IQ

The fatty acids in human milk may boost IQ. Breast-fed infants with at least one copy of a common variant of the gene *FADS2* had IQ scores that were six to seven points higher than those of non-nursed kids with similar genetics. But breast-feeding did not appear to affect those children (10 percent of the study population) with only a less common version of *FADS2*. The gene variants may affect the conversion of dietary precursors to long-chain polyunsaturated fatty acids, which aggregate in the brain after birth. Alternatively, the fatty acids may act on the gene itself, causing it to affect the metabolic processing of the acids. *—Nikhil Swaminathan*

ROBO BUDDY

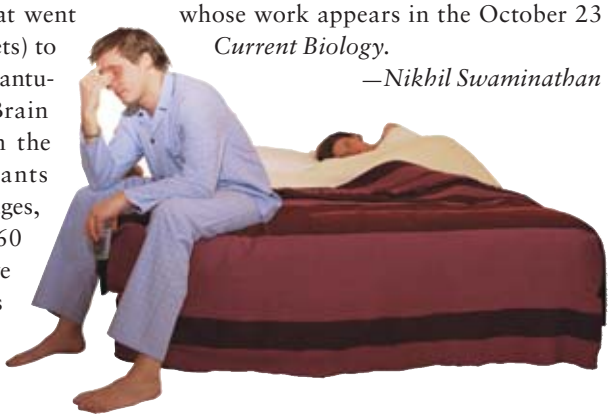
For robots to be accepted as human peers (as Bender is on *Futurama*), it might just take a light touch. Scientists introduced a classroom of toddlers—who naturally had no preconceived notions regarding droids—to a two-foot-tall humanoid robot, QRIO, which giggled when its head was touched. Over time, the children bonded with QRIO, touching it as they did other humans. After five months, the children treated QRIO as a near equal, even covering it with a blanket and telling it "night night" when its batteries ran out. But when the robot was reprogrammed just to dance, the toddlers lost interest. The findings appear in the November 13 *Proceedings of the National Academy of Sciences USA*. *—Charles Q. Choi*

NEUROSCIENCE

Psychiatric Disorders from No Sleep?

Psychiatric problems can trigger sleep issues, and now research suggests the reverse is true—that is, a lack of shut-eye can cause psychological disturbances. Matthew Walker of the University of California, Berkeley, and his collaborators studied 26 volunteers, 14 of whom spent 35 hours without getting a wink. All the subjects then saw photographs that went from benign (wicker baskets) to increasingly disturbing (tarantulas and burn victims). Brain scans revealed that when the sleep-deprived participants viewed more gruesome images, their amygdala showed 60 percent more activity relative to the normal population's response. "The amygdala seems to be able to run amok," Walker says of that forebrain structure that decodes emotion. The boosted activity leads to a pendulum of emotions, from upset and annoyed to giddy, in moments. Among its many other functions, sleep may serve to prepare "our emotional brains for the next day's social and emotional interactions," says Walker, whose work appears in the October 23 *Current Biology*.

—Nikhil Swaminathan



AGRICULTURE

Signs of a Green Revolution

Per capita food production in sub-Saharan Africa is at last rising. According to the World Bank's World Development Report 2008, agricultural growth there "has accelerated from 2.3 percent per year in the 1980s to 3.3 percent in the 1990s and to 3.8 percent per year between 2000 and 2005." That growth has cut poverty rates in 10 of 13 countries analyzed. In addition to lack of drought, these results arose from an African "green revolution" that experts and United Nations officials called for in 2004. It entails relatively simple strategies, such as government subsidies for fertilizers and better crop varieties, so that farmers pay only 25 percent of the actual costs. Moreover, food production has been increasing more than population growth. Problems still persist, though, such as a lack of access to agricultural markets in the developed world. And global pressure to produce biofuels rather than food may mean that hunger will not be erased anytime soon. *—David Biello*

GROWING SUCCESS: Simple measures, such as irrigation with manual pumps, boosted Malawi's food production.

SciAm Perspectives

Congress Fails Science

The Democratic majority continues a legacy of inaction

BY THE EDITORS

The U.S. Congress has long been a slow and irresolute institution, especially when it comes to science issues. Unfortunately, the Democratic majority that came to power in the 2006 midterm election has so far done little to change that reputation. Nearly a year after the Democrats took over the legislative branch, America continues to escalate its emissions of carbon dioxide and other greenhouse gases that are slowly roasting the globe. Furthermore, although Congress has proposed funding increases for many scientific agencies and national laboratories, researchers still have no reassurance that Uncle Sam will actually deliver its promised grants and budgets. Here are some highlights of how the 110th Congress has handled science measures over the past year.

Energy. Promoting energy efficiency and renewable sources is vital to curbing greenhouse gases, but as of early November Congress's much anticipated energy bill was stuck in legislative limbo. In June the Senate passed a promising measure that would raise the fuel economy of cars and light trucks from the current average of 26 miles per gallon to 35 mpg by 2020; in August the House approved a bill that would repeal subsidies for the oil and gas industry and require utilities to produce 15 percent of their electricity from renewable sources such as wind power. Unfortunately, the House and Senate bills were wildly different, and the usual process for reconciling the measures—negotiations in a House-Senate conference committee—broke down. Claiming that Senate Republicans had blocked efforts to appoint committee members, House Speaker Nancy Pelosi of California announced in October that Democratic leaders in the House and Senate would hammer out a compromise. In the face of veto threats from President George W. Bush, will the tough efficiency proposals survive? The chances look dim.

Global warming. As the energy bill falters, Congress has launched a parallel effort to fight global warming by proposing a "cap and trade" system for industrial polluters. Sponsored by Senators John Warner of Virginia and Joseph Lieberman of Connecticut, America's Climate Security Act is aimed at reducing greenhouse gas emissions to 60 percent of current levels by 2050. Although the bill has bipartisan support, it has only just entered the legislative mill and may also face opposition from the White House.

Drug safety reform. One of the modest victories of the 2007 session was a law giving the U.S. Food and Drug Administration more power to monitor the safety of newly introduced pharmaceuticals. Spurred by the Vioxx debacle of 2004, the reform legislation enables the FDA to force drugmakers to conduct long-term studies of drugs whose side effects may not become apparent until they are in widespread use. The law also orders the pharmaceutical industry to pony up $225 million over the next five years to pay for the new safety monitoring.

Science funding. In his State of the Union address last January, President Bush announced the American Competitiveness Initiative, an ambitious plan to beef up federal funding for the physical sciences. Congress responded by significantly boosting the proposed budgets for the National Science Foundation, the National Oceanic and Atmospheric Administration, the National Institute of Standards and Technology, and the U.S. Department of Energy's Office of Science. The extra money would be a particularly great boon for researchers investigating climate change, but because Congress approved the budget increases without cutting funding in other areas, President Bush is now threatening to veto the appropriations bills. Many of the pro-

MATT COLLINS

posed increases may vanish before the bills become law, and in the meantime federal agencies have to operate at last year's funding levels.

Who's to blame? Our government's dismal science record for 2007 is partly the result of the political gridlock that occurs whenever one party controls Congress and the other rules the White House. Last June, for example, President Bush vetoed legislation that would have expanded federal funding for embryonic stem cell research. But some Democratic lawmakers have also obstructed progress. Representative John Dingell of Michigan, chairman of the House Energy and Commerce Committee, fought the increase in fuel economy standards proposed in the Senate's energy bill, saying it would devastate U.S. automakers. Internal divisions among Democrats led to the current logjam on the energy issue, which must be untangled for the sake of our planet. ■

THE EDITORS' BLOG

For more posts from SciAm Observations, see *www.SciAm.com/blog*

Won a Nobel? Go Nuts!

Posted by Philip Yam, October 19, 2007

As a long-time science journalist, I have learned to take what James Watson says with a grain of salt. Even so, I was caught off guard by the outrageousness of his latest words. Watson gets all the kudos for his genetics work, and his discovery with Francis Crick of the double-helical structure of DNA unquestionably deserved the Nobel Prize. But maybe that's what's wrong.

For most research scientists, winning the Nobel Prize stands as the pinnacle of success, the ultimate goal that takes intelligence, dedication, luck and ambition (and don't be fat, Watson would say, because fat folks are not ambitious). Once the king of Sweden drapes that medal around your neck, life is good—people want to hear you speak, offer you prestigious positions and are more inclined to give you what you want.

To their credit, some scientists take the opportunity to tackle very "out there" research. Soon after he won his 1995 Nobel in Physics, Martin Perl launched a project to find "free quarks." Conventional thinking says there can be no such things—quarks must remain bound in the particles in which they build—but some scientists speculate that some quarks might have been left over during the big bang. Perl recognized the long-shot odds of finding these quarks, but it was a project he could do because of his Nobel. A graduate student would be committing career suicide.

Other researchers run from the glory. Brian Josephson, who discovered the quantum effect in which superconducting electrons could jump across a narrow barrier, went off to study mysticism and psychic phenomena. (His problems, though, may run deeper; not many people would choose Taco Bell for a [free] lunch meeting.)

After the wacky things James Watson has uttered over the past decades—on

continued on page 37

Sustainable Developments

Primary Health for All

Ten resolutions could globally ensure a basic human right at almost unnoticeable cost

BY JEFFREY D. SACHS

Sixty years ago at the launch of the World Health Organization, the world's governments declared health to be a fundamental human right "without distinction of race, religion, political belief, economic or social condition." Thirty years ago in Alma Ata, the world's governments called for health for all by the year 2000, mainly through the expansion of access to primary health facilities and services. While the world missed that target by a long shot, we can still achieve it, at remarkably low cost. Ten key steps can bring us to health for all in the next few years.

These simple steps could save the lives of nearly 10 million adults and children.

First, affluent countries should devote 0.1 percent of their gross domestic product to health care for low-income countries. With a rich world GDP of $35 trillion, that would create a fund of roughly $35 billion a year—enough for $35 per capita in added health services for the roughly one billion people who need them.

Second, half the increase should be channeled through the Global Fund to Fight AIDS, Tuberculosis and Malaria. The Global Fund has proved to be a highly effective institution, with minimal bureaucracy and maximum impact. It has supported the distribution of approximately 30 million antimalaria bed nets, helped to get nearly one million Africans on antiretroviral treatment and helped to cure more than two million people of TB.

Third, low-income countries should devote 15 percent of their own national budgets to health. Consider a poor country where the average income is $300 a year. The total national budget might be around 15 percent of GDP, or roughly $45 per capita. Fifteen percent of that figure devoted to health would come to just $6.75 per person per year: not enough to provide adequate basic health care on its own, but combined with $35 per capita from donor aid, it would do the job.

Fourth, the world should adopt a plan for comprehensive malaria control, aim-

BRUCE GILBERT/EARTH INSTITUTE

ing to bring malaria mortality nearly to zero by 2012 through comprehensive access to antimalaria bed nets, indoor spraying where appropriate, and effective medicines when malarial illness arises.

Fifth, the rich countries should follow through on their long-standing and achievable commitment to ensure access to antiretrovirals for all HIV-infected individuals by 2010.

Sixth, the world should fill the financing gap of roughly $3 billion a year for comprehensive TB control—another area where known and long-proved interventions are highly effective but chronically underfunded.

Seventh, the world should honor, for just a few billion dollars a year, the access of the poorest of the poor to sexual and reproductive health services, including family planning, contraception and emergency obstetrical care.

Eighth, the Global Fund should offer roughly $400 million a year for comprehensive control of several tropical diseases (mainly worm infections), which occur in virtually the same regions where malaria is rampant.

Ninth, the Global Fund should open a new financing mechanism to bolster primary health care, including—most important—the construction of clinics and the hiring and training of nurses and community health workers.

Tenth, using recent breakthroughs in medicine and public health, the expanded health systems in the poorest countries should be equipped to handle noncommunicable diseases that have long been neglected but are treatable at low cost: hypertension, cataracts and depression.

These simple steps could save the lives of nearly 10 million adults and children a year, at a cost that would be nearly unnoticeable to the world's wealthiest nations. These measures would also slow, rather than accelerate, population growth in impoverished regions, thereby easing the economic and environmental strains that bulging populations are imposing on them. Health for all is not only the moral imperative it was at the launch of the World Health Organization 60 years ago, it is also the best practical bargain on the planet. ■

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

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

Forum

A Better Mosquito Net

Fighting malaria will require more innovative defenses

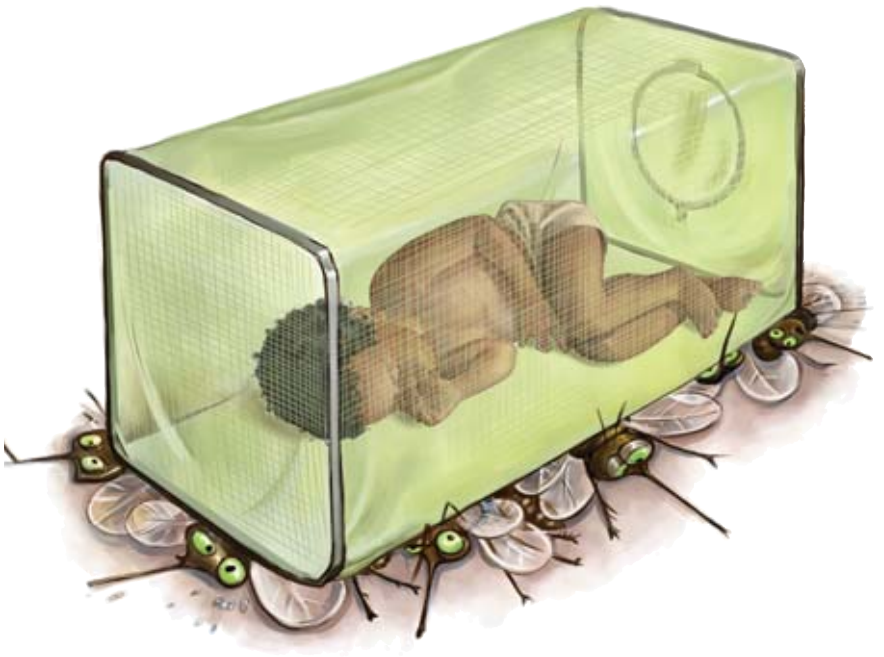
BY EVA KAPLAN

Malaria remains one of the world's great scourges, striking more than 500 million people every year. The groups most at risk are pregnant women and children younger than five years old. In sub-Saharan Africa, 20 percent of all childhood deaths are from malaria. Pregnant women who contract the mosquito-borne disease can develop severe anemia and give birth to underweight babies. The World Health Organization estimates that 10,000 pregnant woman and 200,000 infants in Africa die from malarial infections every year.

To combat the disease, many development agencies have focused on distributing mosquito nets that would protect Africans from being bitten while they sleep. This strategy has resulted in a huge upsurge in the number of bed nets supplied to the population as a whole and particularly to pregnant women and young children. The widespread distribution, however, has *not* resulted in a significant decrease in malaria. Many doctors in sub-Saharan Africa attribute the failure to an overreliance on nets in lieu of other interventions, such as the indoor spraying of dwellings with insecticide. Other experts say the problem is the misuse of mosquito nets; there is anecdotal evidence that some people have employed the nets as wedding veils or fishing aids. Some economists argue that charging a small fee for the nets would increase the likelihood that they would be used appropriately. Others claim such a fee would prevent a large part of the population from receiving nets. These are valuable debates. Before delving into behavioral economics, though, it might be useful to consider a more basic problem: the mosquito nets are poorly designed.

The bed nets distributed by governments and international organizations have one of two basic designs: circular or

PHOTOGRAPH BY JAMES BORLAND; ILLUSTRATION BY MATT COLLINS



MATT COLLINS

rectangular. The circular design hangs from the ceiling by one string, with the net fanning out from a ring at the top and tucked tightly under the mattress on all sides. The rectangular design ties to the ceiling with four strings and hangs straight down on all sides of the bed, with the fringes again tucked under the mattress. Both designs work well for middle-class homes with flat ceilings and a bed for every member of the family. But most of the poor in sub-Saharan Africa, especially in rural areas, live in mud huts, often with thatched roofs.

Hanging mosquito nets is very difficult in these homes, and most people prefer the circular nets because they are easier to hang. Although the rectangular nets can be used without a bed, the circular nets cannot, because they have to be tucked under the mattress to fan out. In many African communities, most children younger than five sleep on the floor, so only the rectangular nets would be effective. But the rectangular nets take up quite a bit of room in a mud hut and have to be taken down and rehung every night for the hut to be of use during the day. Given the difficulty of hanging the nets, it is unreasonable to expect people to follow this routine.

A design more suited to the needs of young children would be a net that does not hang at all. One possibility would be a collapsible, tentlike structure, very similar to the crawl-through children's toys that clutter so many playrooms in the U.S. The challenge would be to make the structure both affordable to produce and durable enough to be used daily for years. In addition to being user-friendly, this free-standing mosquito net would have to be sized for children to ensure that it is used by the intended recipients rather than older, hardier members of the family.

Mosquito nets have been changed before to meet user needs. Several companies have recently introduced nets that are impregnated with long-lasting insecticide, eliminating the need for people to continually apply fresh coatings of chemicals to the nets. Companies must continue to improve mosquito nets if progress is to be made in combating malaria. And once better nets are available, researchers will be able to objectively judge the effectiveness of the distribution programs. ■

Eva Kaplan is a writer and consultant who has managed research projects focused on disease prevention in sub-Saharan Africa.

THE EDITORS' BLOG

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women, homosexuals and the obese, to name a few—now comes his decision to join hands with the transistor-developing, eugenics-advocating, sperm-donating William Shockley, who, I recall, blamed his wife's genes for his kids being less than genius. As a geneticist, Watson arguably has better credentials to rant about race and IQ than Shockley. But that still doesn't make him an expert on IQ studies. It's true that blacks have historically scored 15 points lower than whites on IQs. What's been debated endlessly is how much is tied to heredity and how much to environment. Intelligence researchers such as James Flynn have found that IQ can change over time, suggesting a strong environmental influence. Others, such as Philippe Rushton and Linda Gottfredson, say the data are at least as consistent with hereditarian arguments as they are with environmental ones. I don't want to get into a whole discussion about IQ again—we've covered it a lot in this magazine (see, for instance, "Unsettled Scores" [February 2007] and our Intelligence special issue [*Scientific American Presents,* Winter 1999]). But while I'm at it, one question I have for the hereditarians: How do you separate genetic explanations from womb conditions—a crucial environmental factor?

Without having mucked around in the morass that is IQ research, Watson can at best be only a casual observer. He's reportedly dim about the prospects of Africa because of that continent's lower intelligence test scores. What—cultural conflicts, religious attitudes and greed are less important? That's hard to justify when you look at what's going on in different parts of the world right now.

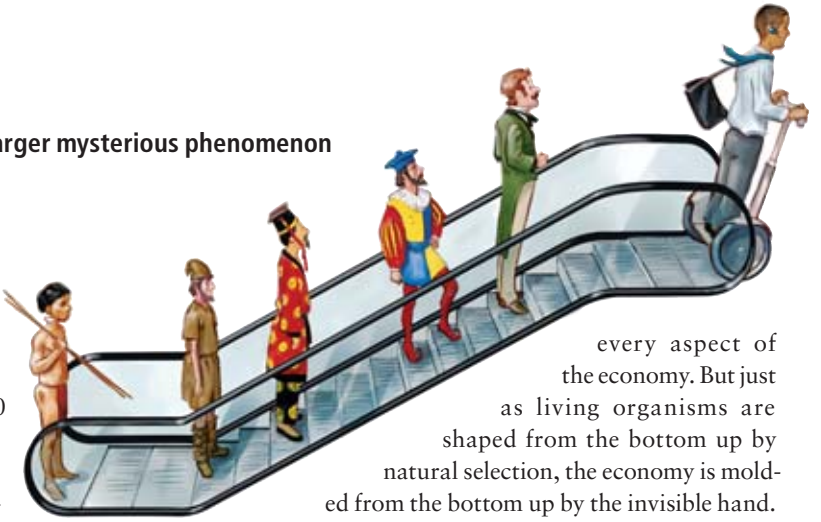
Yet because of his Nobel and past accomplishments as a geneticist, Watson's words take on added meaning and weight beyond what they deserve. Winning the Nobel grants a great deal of power. Too bad Watson didn't channel Stan Lee and recognize that with great power comes great responsibility.

Skeptic

Evonomics

Evolution and economics are both examples of a larger mysterious phenomenon

BY MICHAEL SHERMER



Living along the Orinoco River that bor-ders Brazil and Venezuela are the Yanomamö people, hunter-gatherers whose average annual income has been estimated at the equivalent of $90 per person per year. Living along the Hudson River that borders New York State and New Jersey are the Manhattan people, consumer-traders whose average annual income has been estimated at $36,000 per person per year. That dramatic difference of 400 times, however, pales in comparison to the differences in Stock Keeping Units (SKUs, a measure of the number of types of retail products available), which has been estimated at 300 for the Yanomamö and 10 billion for the Manhattans, a difference of 33 million times!

How did this happen? According to economist Eric D. Beinhocker, who published these calculations in his revelatory work *The Origin of Wealth* (Harvard Business School Press, 2006), the explanation is to be found in complexity theory. Evolution and economics are not just analogous to each other, but they are actually two forms of a larger phenomenon called complex adaptive systems, in which individual elements, parts or agents interact, then process information and adapt their behavior to changing conditions. Immune systems, ecosystems, language, the law and the Internet are all examples of complex adaptive systems.

In biological evolution, nature selects from the variation produced by random genetic mutations and the mixing of parental genes. Out of that process of cumulative selection emerges complexity and diversity. In economic evolution, our material economy proceeds through the production and selection of numerous permutations of countless products. Those 10 billion products in the Manhattan village represent only those variations that made it to market, after which there is a cumulative selection by consumers in the marketplace for those deemed most useful: VHS over Betamax, DVDs over VHS, CDs over vinyl records, flip phones over brick phones, computers over typewriters, Google over Altavista, SUVs over station wagons, paper books over e-books (still), and Internet news over network news (soon). Those that are purchased "survive" and "reproduce" into the future through repetitive use and remanufacturing.

As with living organisms and ecosystems, the economy looks designed—so just as humans naturally deduce the existence of a top-down intelligent designer, humans also (understandably) infer that a top-down government designer is needed in nearly every aspect of the economy. But just as living organisms are shaped from the bottom up by natural selection, the economy is molded from the bottom up by the invisible hand.

The correspondence between evolution and economics is not perfect, because some top-down institutional rules and laws are needed to provide a structure within which free and fair trade can occur. But too much top-down interference into the marketplace makes trade neither free nor fair. When such attempts have been made in the past, they have failed—because markets are far too complex, interactive and autocatalytic to be designed from the top down. In his 1922 book, *Socialism,* Ludwig von Mises spelled out the reasons why, most notably the problem of "economic calculation" in a planned socialist economy. In capitalism, prices are in constant and rapid flux and are determined from below by individuals freely exchanging in the marketplace. Money is a means of exchange, and prices are the information people use to guide their choices. Von Mises demonstrated that socialist economies depend on capitalist economies to determine what prices should be assigned to goods and services. And they do so cumbersomely and inefficiently. Relatively free markets are, ultimately, the only way to find out what buyers are willing to pay and what sellers are willing to accept.

Evonomics helps to explain how Yanomamö-like hunter-gatherers evolved into Manhattan-like consumer-traders. Nineteenth-century French economist Frédéric Bastiat well captured the principle: "Where goods do not cross frontiers, armies will." In addition to being fierce warriors, the Yanomamö are also sophisticated traders, and the more they trade the less they fight. The reason is that trade is a powerful social adhesive that creates political alliances. One village cannot go to another village and announce that they are worried about being conquered by a third, more powerful village—that would reveal weakness. Instead they mask the real motives for alliance through trade and reciprocal feasting. And, as a result, not only gain military protection but also initiate a system of trade that—in the long run—leads to an increase in both wealth and SKUs. ■

Michael Shermer is publisher of Skeptic *(www.skeptic.com). His latest book is* The Mind of the Market *(Times Books).*

PHOTOGRAPH BY BRAD SWONETZ; ILLUSTRATION BY MATT COLLINS

Anti Gravity

What's in a (Latin) Name?

The special genius behind the species and genus

BY STEVE MIRSKY

The greater roadrunner is officially classified as *Geococcyx californianus*. The lesser roadrunner is *Geococcyx velox*. And the more familiar cartoon Road Runner (beep beep) has been designated on different occasions as *Accelerati incredibilus, Velocitus tremenjus, Birdibus zippibus, Speedipus rex* and *Morselus babyfatious tastius*. Consistently unsuccessful in his attempts to catch *Fastius tasty-us* is Wile E. Coyote, himself variously classified as a representative of the species *Carnivorous slobbius, Eatius birdius, Overconfidentii vulgaris, Poor schinookius* or *Caninus nervous rex*. (Real coyotes are *Canis latrans,* which sounds like a bathroom used by Roman legionnaires.)

So who do we, and the Looney Tunes folks, have to thank for setting the ground rules that led to all this highfalutin Latinate humor? None other than Swedish naturalist Carl Linnaeus, who was so in love with naming things that he gave himself a few more: Carl Linné, Carl von Linné, Carolus Linnaeus and Caroli Linnaei, the name by which he proposed the standard genus-species system of taxonomic binomial nomenclature still used to keep track of all that life out there. The year 2007 was the tricentennial of Linnaeus's birth, which shows that some people's contributions give them a postmortem vita that's not at all *brevis*.

American journalist and wag H. L. Mencken paid unwitting tribute to Linnaeus's classification scheme when he dubbed a large percentage of the U.S. population *Boobus americanus*. (Don't worry, he meant the other guys, not you.) Mencken described the perpetually bamboozled *B. americanus* as "a bird that knows no closed season," which coincidentally describes the Road Runner, also known as *Disappearialis quickius*. Mencken, by the way, covered the famous Scopes trial, in which some *Homo sapiens* treated the notion that they were related to *Gorilla gorilla* and *Pan troglodytes* like it was a *Yersinia pestis* infection.

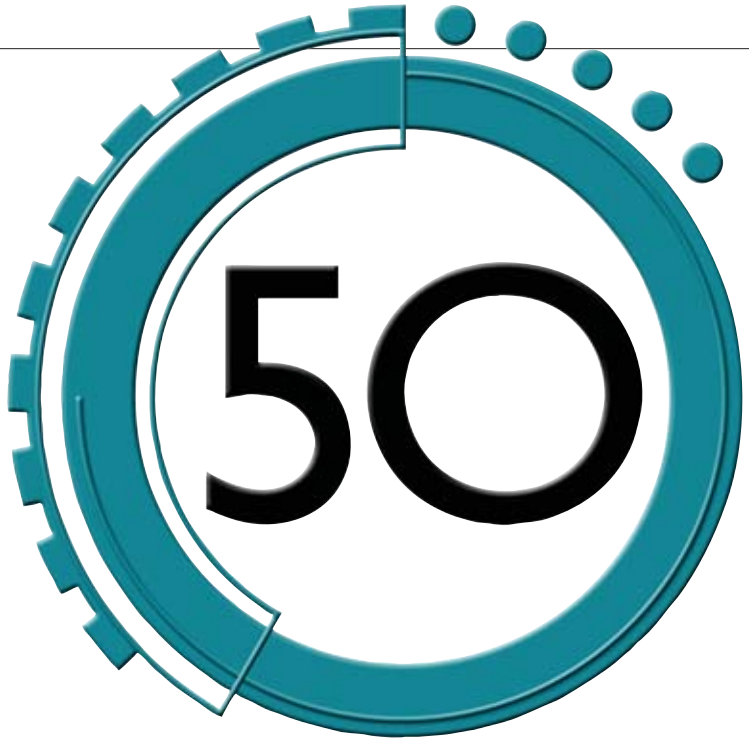
Among Mencken's many pithy comments about *H. sapiens* is, "An idealist is one who, on noticing that a rose smells better than a cabbage, concludes that it will also make better soup." And in fact, mixing up any of the numerous species of the genus *Rosa* with *Brassica oleracea* (Capitata Group) is even nuttier (*Bertholletia excelsa*) in Latin. Preventing mix-ups is one reason why Linnaeus's system comes in so handy: French president Nicolas Sarkozy might call it a *moineau,* Spain's King Juan Carlos might call it a *gorrión,* and Vice President Dick Cheney might (or might not) call out "fire in the hole" before trying to blow it out of the sky, but the bird in question would be recognizable to all their science advisers as *Passer domesticus*. Which is also known in English as the house sparrow. And because common species names, even within a single language, lack the authority of the official Linnaean designations, the house sparrow is also known in English as the English sparrow. Help, is there a taxonomist in the house?

Linnaeus's twin great works were the 1753 *Species Planterum,* in which he classified all the known species of vegetation, and the 1758 *Systema Naturae,* which celebrates its 250th anniversary this year and which was the first major effort at organizing the animal world. The Wikipedia entry on Linnaeus notes that because of his habit of naming all the living things he encountered, "he thought of himself as a second Adam." The cover of *Systema Naturae* shows a man, presumably Linnaeus, tossing Latin titles to "new creatures as they are created in the Garden of Eden." No shrinking member of the genus *Viola* was he.

Linnaeus appears to have occasionally abused his absolute appellative power. The New York Botanical Garden, which hosted a rare public display of Linnaeus's own annotated copy of the *Systema Naturae* last November, notes on its Web site that "he got revenge on his critics by naming unpleasant plants and animals after them. For example, he named *Siegesbeckia,* an unattractive Asian weed that exudes foul-smelling liquid, for German botanist Johan Siegesbeck." So Linnaeus was probably a pain in the *Equus asinus*. But without him, biology could not have become big-name science. ■

PHOTOGRAPH BY FLYNN LARSEN; ILLUSTRATION BY MATT COLLINS

SCIENTIFIC AMERICAN



TRENDS

- Wireless Power
- Drug Delivery
- Sustainable Fuels
- Toxic Housewares
- Ultrameasurement
- Malaria-Free Mosquitoes
- Bioinspired Materials
- Diagnosing Alzheimer's
- Optical Chips
- Prion Disease Treatments
- Sun Power
- Understanding Stem Cells
- Chip Printers
- Prosthetics
- Intelligent Route Finders

Technological overoptimism lurks as a persistent risk to both professional and amateur watchers of advances, from artificial intelligence to the flying car. But sometimes new technologies actually live up to some of the wildest expectations for them.

This year's SciAm 50 awards are replete with instances of new machines or chemicals that come close to the true meaning of innovation as something entirely new. One winner has created an instrument that measures fluids in zeptoliters, or sextillionths of a liter. (You know, the zeptoliter, the measurement unit that is 1,000th of an attoliter?)

Another innovator has devised a method that could recharge a phone without plugging it in. All you would have to do is sit at the dining room table, phone in pocket, a few feet away from a recharging coil hidden in the ceiling. Still another visionary is paving the way for treating mysterious and deadly prion diseases such as mad cow and kuru.

Award winners highlighted here have the potential to contribute much more to human health, consumer electronics and numerous other fields than if they were simply offering another antidepressant that tweaked serotonin levels or ratcheting up the speed of a microprocessor. What they have done is decidedly new.

—The Editors

The Wellcome Trust Case Control Consortium

U.K.

A massive genetic study turns up the complex roots of major diseases

With genetic scientific advances reported almost daily, it sometimes seems as if we are merely waiting for researchers to discover the gene at fault for every human disease. The complex genetic basis of many common diseases, however, complicates prediction, diagnosis and treatment.

The Wellcome Trust Case Control Consortium (WTCCC), a constellation of more than 50 British research groups, took on the mammoth challenge of ferreting out the causes of diseases in which multiple genes are implicated. Last June they reported the findings of a study that scanned for specific gene variations among 17,000 British citizens: 2,000 each from patient groups diagnosed with bipolar disorder, coronary heart disease, Crohn's disease, rheumatoid arthritis, hypertension and diabetes types 1 and 2, as well as 3,000 unafflicted who served as a control group. The large scale of the study was unprecedented and so was the payoff: 24 locations in the genome were found to be associated with six of the seven diseases.

The WTCCC compared the genomes of each affected group with those of the controls and zeroed in on locations where DNA bases differed between the two groups. The size of the study was essential in enabling the researchers to spot rare anomalies. Some of the signals were in coding regions of genes; some were in noncoding regions that might regulate other genes; and some were in "gene deserts"—noncoding regions with no identified function. The variants themselves may not actually be responsible for the diseases. But they serve as signposts for other researchers to investigate DNA at a fine scale.

Every person possesses a certain pattern of "polymorphisms" in the six billion nucleotides of their genomic DNA—three billion for each of the two sets of chromosomes. The statistical pattern of how these variations occur, provided by studies such as the one conducted by the WTCCC, will help physicians calculate the chances that a patient could develop symptoms of a hereditary disorder. The ultimate goal of this research is personalized medicine in which patients submit a blood sample and have their entire set of genes analyzed to determine predisposition to chronic diseases, the best food and exercise regimens to stay healthy, and which drugs and dosages will be most effective when illness does strike. —*Kaspar Mossman*

GENOME-WIDE SCANS turned up gene variants associated with disease, such as those for type 1 diabetes, shown as green highlights on a representation of chromosomes.

FROM "GENOME-WIDE ASSOCIATION STUDY OF 14,000 CASES OF SEVEN COMMON DISEASES AND 3,000 SHARED CONTROLS," BY THE WELLCOME TRUST CASE CONTROL CONSORTIUM, IN *NATURE*, VOL. 447; JUNE 7, 2007. REPRINTED BY PERMISSION OF MACMILLAN PUBLISHERS LTD. (*top*); THOMAS DEERINCK *NCMIR/Photo Researchers, Inc.* (*bottom*)

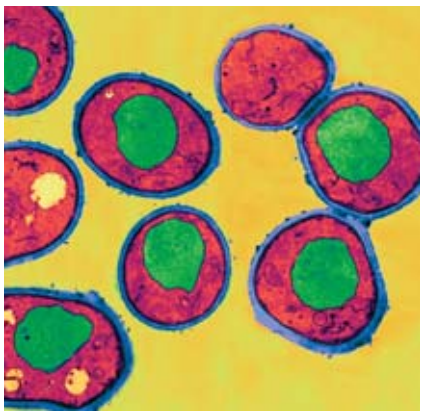
Amyris Biotechnologies

Emeryville, Calif.

The emerging field of synthetic biology provides candidates for a new generation of biofuels

Ethanol is not the most energy-dense of fuels nor the cheapest. Consequently, Amyris Biotechnologies in Emeryville, Calif., has come up with a potentially better solution. It did so by starting with a long roster of organic compounds from which it chose potential replacements for gasoline, diesel and jet fuel that could be burned in modern engines and would be compatible with the existing petroleum infrastructure. Then the company used custom-designed microbes to produce the new fuels by fermentation from a conventional ethanol feedstock.

To create the novel strains was no small genetic feat. The task required sub-



YEAST microbes, once genetically engineered, can boost biofuel yields dramatically.

stantial alterations to the yeast genome. Genes from the original plant source and two other organisms were inserted, and a preexisting biochemical pathway was carefully adjusted. The engineered yeast boasted a millionfold increase in yield.

A leader in the emerging field of synthetic biology, Amyris is well known for developing a strain of yeast for large-scale manufacture of a precursor to the antimalarial drug artemisinin, for which the Asian plant source is in short supply. The company, chosen in 2006 by the World Economic Forum as a Technology Pioneer, is now close to its goal of supplying cheap industrial quantities of artemisinin to developing countries.

Amyris decided that its expertise could prove equally profitable when applied to biofuels. It initiated a search for fuels that could be produced in the lab and that met criteria on energy content, volatility and water solubility.

The difference between engineering microbes to produce drugs versus fuel is that, ounce for ounce, drugs are much more valuable: a fuel end product has to be cheap enough to burn. Amyris will have to optimize each microbial strain so that it cranks out fuel without poisoning itself and produces enough fuel molecules so that it is economically worthwhile to grow. In the history of the large-scale chemical industry, the subtlety of technical expertise involved in this project is without precedent. Yet Amyris, which last June added several oil industry veterans to its management, has shown that it means business. —*Kaspar Mossman*

SciAm 50 POLICY LEADER OF THE YEAR

X Prize Foundation

Santa Monica, Calif.

The lure of multimillion-dollar prizes prompts inventors to pursue breakthroughs in space travel, DNA sequencing, automotive fuel efficiency, and robotics

In 1927 the aviation world marveled at Charles A. Lindbergh's nonstop flight from New York to Paris. Lindbergh was in it for more than thrills: he was after the $25,000 Orteig Prize. In a 21st-century encore, the 12-year-old nonprofit X Prize Foundation conceives and manages competitions for daring innovators.

The foundation's game plan is to define an exciting target that benefits humanity, bait it with a large stack of cash, and draw out the best in design and invention from private, nongovernmental teams. The competitors, the thinking goes, will invest much more in technology chasing the prestige of the prize than the foundation will hand out at the awards ceremony.

Events have borne out this prediction. The foundation set a goal in 1995 "to make space travel safe, affordable and accessible to everyone through the creation of a personal spaceflight industry." In 2004 Mojave Aerospace Ventures won the Ansari X Prize as the first team to build a space plane that could reach low-Earth orbit, return to Earth and repeat the flight within two weeks. Twenty-six teams entered the contest and collectively spent more than $100 million on research.

The second prize, which the foundation offered in late 2006, is the $10-million Archon X Prize, for the first private team to sequence 100 human genomes in 10 days at a cost of less than $1 million. At least four teams have already signed up for the challenge of inventing an instrument that will correctly sequence 98 percent of each genome with no more than 60,000 errors.

The winning technology would accelerate deployment of new discoveries such as genome-wide association studies, which analyze large patient groups to identify genes responsible for complex hereditary diseases. A prominent supporter of the Archon X Prize is Stephen Hawking, the renowned theoretical physicist who suffers from amyotrophic lateral sclerosis.

Last April the foundation also offered the Automotive X Prize, for the first 100-mile-per-gallon production car. And in September the group announced the $30-million Google Lunar X Prize purse for the first private groups to land spacecraft on the moon. Money may be an object for some, but there is no doubt that the challenges set by the X Prize Foundation light a fire under innovators worldwide. —*Kaspar Mossman*

AMBITIOUS GOALS that benefit humanity, such as a private robotic moon mission, serve as the rationale for the X Prize Foundation.

COURTESY OF X PRIZE FOUNDATION

Connections to an Untethered Future

Delivering electric power through the air cuts the final cord

Although laptops, cell phones and other gadgets give us remarkable mobility, we can roam untethered only for as long as our batteries hold out. Photonics researcher Marin Soljačić of the Massachusetts Institute of Technology wants to eliminate that shackle by delivering wireless electricity, or WiTricity.

Soljačić hung a copper coil 0.6 meter (two feet) in diameter from a ceiling, then hung another coil about 2.1 meters (seven feet) away, with a 60-watt lightbulb dangling from it. When he plugged the first coil into a power source, the lightbulb on the second coil lit up. Electric current in the first coil established a magnetic field that induced current in the second one.

The iPhone's "multi-touch" screen gives the user access to a standard keyboard, streaming video, music and a list of voice mails.

Many motors exploit this effect, but normally induction works only across gaps of a few millimeters, dying off rapidly with greater distance. Soljačić tuned his coils to resonate, allowing efficient energy exchange over a distance. Future implementations of his system might enable laptops and cell phones to recharge when they are in a room equipped with a resonance emitter.

The human impulse to cut the cord runs deep. Apple released the iPhone as an ultimate wireless interface, and people lined up to pay $600 for it. The handheld device combines all the functions of an advanced mobile phone with those of the latest iPod, thereby allowing users to wander freely while making phone calls, accessing the Web, sending text messages and e-mail, taking photographs, listening to music and watching videos. Although some earlier phones had offered many of these functions, the iPhone's full-size "multi-touch" screen gave customers far more flexibility, including use of a standard keyboard for messaging, streaming of YouTube video and a visual list of voice mails—not to mention access to iTunes, by far the dominant online music source.

Wireless sensors also gained flexibility. Reduced to the size of rice grains or dust, they can mount a vigil for chemical and biological weapons or check for moisture content in the soil. Already they are changing how people monitor the world. A major barrier, however, has been how to know if such networks of randomly distributed sensors leave gaps in coverage or if the sensors' ranges overlap, thus wasting the precious bits of power they may carry.

Robert Ghrist, a mathematician at the University of Illinois at Urbana-Champaign, and mathematics professor Vin de Silva of Pomona College harnessed the science of mathematical homology to answer both questions. Homology analyzes the points, lines and geometric arrangements within shapes. By treating sensors as points, pairs of sensors as edges, and collections of edges as shapes, Ghrist and de Silva devised algorithms that can tell whether a sprinkled network of sensors overlap or leave gaps.

The advantage of Ghrist's and de Silva's algorithms is that they only need to know which sensors are within range of one another, not where each sensor actually is; they eliminate the need for expensive global-positioning circuits or the manual mapping of circuits. Knowing the locations of gaps and overlaps, network operators could turn up the power of certain sensors or strategically add new ones to fill in blank spots. —*Mark Fischetti*

Getting from Here to There

A protein borrowed from the rabies virus gets a drug to where it is needed

As hard as it is for scientists to develop new drugs, sometimes just getting the drug to where it needs to act is equally challenging. Nowhere is this more true than in the brain, where blood vessel walls are tightly knit, keeping most large molecules from seeping out of the bloodstream and into brain tissue. This blood-brain barrier is a formidable obstacle to delivering certain types of treatments for neurological diseases, but Manjunath N. Swamy and his team at Harvard Medical School's Immune Disease Institute devised a clever way to sneak a drug through and insert it directly into brain cells.

Some viruses that specialize in infecting the nervous system, such as rabies and herpes, are adept at penetrating the blood-brain barrier. Swamy's group exploited that capability by disguising a drug with a small protein normally found

on the surface of the rabies virus. The protein is believed to unlock a passageway through the blood vessel walls, and a drug molecule hitched to the viral protein was able to penetrate the barrier. Once inside the brain, the protein also allowed the drug to enter individual nerve cells, much as a virus would infect them. The therapeutic molecule used in Swamy's experiments was a small nucleic acid chain, known as a short-interfering RNA (siRNA), which can be customized to target specific genes and suppress their effects, making siRNA delivered straight to the brain a versatile tool for a wide range of uses.

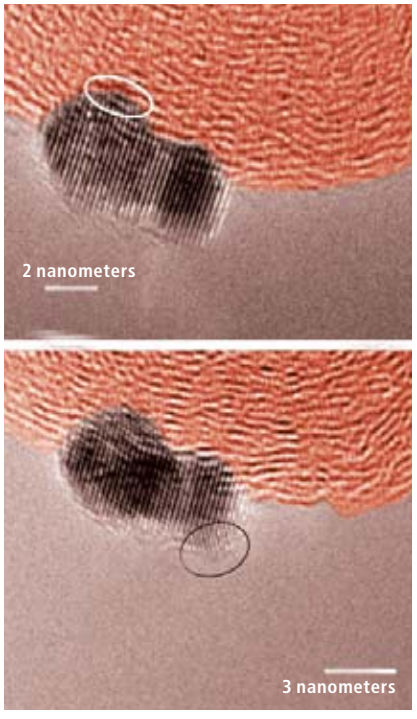
The same can be said of another tiny Trojan horse built by Hans Boumans and his colleagues at the Netherlands Organization for Applied Research. The team's "BioSwitch" consists of a biopolymer cage that can protect or conceal a variety of substances until their release is desirable. Both the cage material and the trigger to discharge its contents can be tailored to specific situations.

For instance, Boumans's group created a germ-killing plastic wrap for meat by encapsulating a bactericidal enzyme inside woven cages of cross-linked starch molecules, then coating the plastic with them. The starch cages remain inert unless bacteria are present and start eating the starch, thus degrading the cage until—surprise—the killer enzyme is released. A similar system could allow unstable food-flavoring molecules to remain encased until they contact enzymes on the tongue or foul-tasting nutrients to stay sealed in their cages until they reach digestive enzymes in the gut. —*Christine Soares*

Fueling Alternatives

Engineers make progress toward new green fuels and energy storage devices

Despite efforts to brew ethanol as a sustainable automotive fuel substitute for gasoline, the plant-derived alcohol has its drawbacks. A gallon (3.8 liters) of ethanol, for one, contains almost a third less energy than the same volume of gasoline.



Gold clusters (*circles*) retard the oxidation of a platinum catalyst in a fuel cell.

FROM "STABILIZATION OF PLATINUM OXYGEN REDUCTION ELECTROCATALYSTS USING GOLD CLUSTERS," BY J. ZHANG, K. SASAKI, E. SUTTER AND R. R. ADZIC, IN *SCIENCE*, VOL. 315; 2007. REPRINTED WITH PERMISSION OF AAAS

So when James A. Dumesic and his fellow chemical engineers at the University of Wisconsin–Madison developed a straightforward way to extract a synthetic fuel from sugar that in many ways surpasses ethanol, the scientific community took notice. Called 2,5-dimethylfuran, or simply DMF, the fuel possesses an energy density equivalent to that of gasoline. It is also insoluble in water and stable in storage. Although chemists have long known about the compound, volume production has been tricky. The new two-step process makes improvements in an intermediate manufacturing step that was a barrier to mass production of DMF.

Beyond finding new alternative fuels for internal-combustion engines, researchers are working on fuel cells that offer another path toward environmentally acceptable power. The key to an effective hydrogen, or proton-exchange membrane (PEM), fuel cell is the microthin coating of platinum particles on the positively charged electrode, where oxygen molecules split into individual charged atoms.

Chemist Radoslav R. Adzic and his team at Brookhaven National Laboratory have found a way to stop the platinum on the electrode's surface from oxidizing, which slows down power-generating chemical reactions and also often causes its membrane to degrade, rendering the cell useless. By spraying the electrode with nanoparticles of gold, Adzic's team made the platinum layer resistant to dissolving and helped it retain most of its original catalytic efficacy.

To produce electricity, most PEM fuel cells must be supplied either with hydrogen or with hydrocarbon compounds that can be catalytically decomposed into hydrogen. Some prototype fuel cells, however, resemble biological cells in that they use chemical enzymes to break down sugars—a special class of hydrocarbon molecules—to generate electrons. Unlike living cells, they typically soon run out of the enzymes necessary to sustain the reaction.

Electrochemist Shelley D. Minteer and her colleague Tamara Klotzbach, both at Saint Louis University, have developed a method to replenish the enzymes in a sugar-powered fuel cell as they degrade with use. The researchers have come up with a polymer wrapping for an enzyme, which keeps the catalytic molecule active for months instead of days.

—*Steven Ashley*

Fighting Toxins in the Home

Everyday materials may pose health and environmental threats

Ordinary plastic items may cause sickness.

Researchers are continually finding new evidence that common items in our kitchens, bathrooms and toy chests can make us sick. One of the most insidious substances is bisphenol A, a component of the light plastics used in baby bottles and many other consumer products. Over the past several years, scientists have reported that low levels of bisphenol A can disrupt cell division, leading to spontaneous miscarriages and birth defects such as Down syndrome.

In early 2007 a team led by Patricia A. Hunt of Washington State University found that small amounts of bisphenol A interfered with the growth of egg cells in developing female mouse embryos. As many as 40 percent of the eggs from fetuses exposed to bisphenol A had an abnormal number of chromosomes. This stunning finding showed that the chemical's effects can run through three generations: the pregnant mother's exposure damages the daughter's reproductive cells, which in turn disrupts the development of the daughter's own children.

The National Toxicology Program, which is part of the National Institutes of Health, is currently reviewing the safety of bisphenol A. In the meantime, some physicians advise pregnant women to avoid drinking water from plastic bottles, especially once the containers become visibly scratched or scuffed, which may indicate that they are leaching the hazardous chemical.

Toxic household items also pose a danger to the environment. Unused pharmaceuticals are a particularly serious threat because consumers often flush them down the toilet, sending the potent molecules into rivers and lakes. Discarded birth-control pills can trigger reproductive problems in fish, and surplus antibiotics can enhance the spread of bacteria that are resistant to the drugs. In an attempt to tackle this problem, the American Pharmacists Association and the U.S. Fish and Wildlife Service signed an agreement last year to launch a public-awareness campaign to change consumer habits. When people pick up their prescriptions, they will be advised to dispose of their unused pharmaceuticals through hazardous-waste collection programs. If such programs are not locally available, the next best option is crushing and diluting the medicines, then sealing them in plastic bags and dumping them in the trash. (Some narcotic drugs will be exempt from the recommendations because of the risk that addicts will retrieve the pills from garbage cans.)

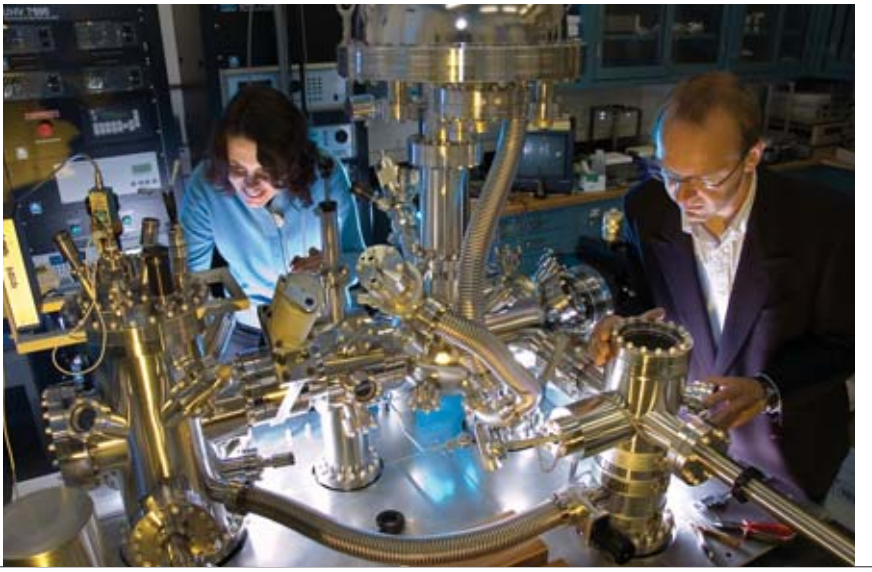
An even better solution would be the establishment of incentives to encourage consumers to return their unused drugs to pharmacies. Pilot programs of this type are now operating in California, Washington State and Maine. —*Mark Alpert*

Advances in Ultrameasurement

Zeptoliter pipettes and quantum rulers give new meaning to the word "small"

Scientists use pipettes when they need to dispense well-defined volumes of liquid. Existing pipettes can deliver fluid volumes as small as an attoliter—a quintillionth, or a billionth of a billionth, of a liter.

Physicists Peter W. Sutter and Eli A. Sutter of Brookhaven National Laboratory have broken that lower limit by constructing a pipette that metes out a droplet measured in a unit that is a thousandth as small—a zeptoliter (a sextillionth of a liter). Such a minute volume



Eli A. Sutter and Peter W. Sutter built the world's smallest pipette, which helped to show that droplets of liquid metal freeze differently than scientists expected.

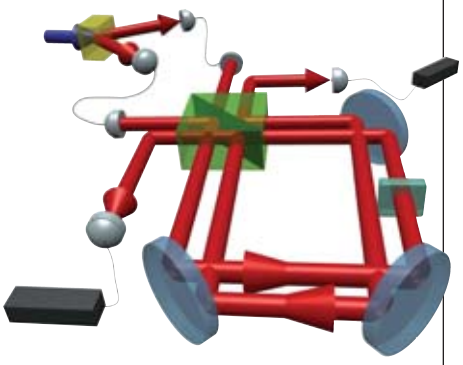
KRISTY-ANNE GLUBISH *Design Pics/Corbis (top)*; COURTESY OF BROOKHAVEN NATIONAL LABORATORY *(bottom)*

can contain as little as 10,000 to as much as a million atoms of metal.

The researchers used a germanium nanowire with a solid reservoir of gold-germanium alloy at one end. They encapsulated the two-micron-long assembly in a carbon shell, which constituted the pipette. Inside a vacuum chamber, they heated and melted the alloy and then aimed an electron beam at the shell's tip. The beam bored an escape hole for the molten metal, which formed a minuscule droplet up to 40 nanometers in diameter and 35 zeptoliters in volume.

If measuring things in zeptoliters is difficult, consider doing so at a scale where the rules of classical physics cease to prevail. Quantum metrology—the field in which quantum mechanics is used to obtain highly precise measurements—has allowed physicists at Hokkaido University in Japan and the University of Bristol in England to almost double the precision of measurement when using photons to gauge distances.

The scientists have built on previous work that uses photons "entangled" in the same quantum superposition of states. The team directed two photonic pairs into an interferometer—an instrument that creates a circular beam path with mirrors in which light waves interfere with one another. Each photon splits, taking separate paths simultaneously. Four photons in an entangled state circulate around the interferometer in one direction, and another quadruplet traverses the loop in the other. The interference produced by the countercirculating photons reveals tiny differences in how far each quadruplet has traveled.



Entangled photons in an interferometer make ultraprecise measurements.

The precision measurements could, for example, be useful when using lasers to etch ultrathin circuits on computer chips. —*Steven Ashley*

Mosquitoes Enlisted to Beat Malaria

Bugs engineered to avoid transmitting the disease could outcompete bugs that do transmit it

Malaria still kills more than a million people a year. Even though low-tech measures such as spraying insecticides and distributing treated bed netting to residents can reduce infection rates, poor countries, where most victims live, cannot afford them.

As an alternative strategy, researchers have tried for years to genetically engineer mosquitoes so they will not transmit the disease. Malaria is caused by protozoan parasites that reproduce inside human liver and red blood cells and are passed from person to person by female *Anopheles* mosquitoes. Although several research teams managed to insert genes into lab-bred mosquitoes that made the bugs less hospitable to the parasites, the altered strains did not reproduce or survive as well as wild strains did.

But last March microbiologist Marcelo Jacobs-Lorena of Johns Hopkins University announced results indicating that engineered insects could outsurvive wild ones. Jacobs-Lorena inserted a gene into *Anopheles* that directs production of a peptide called SM1, which manifests in the mosquito's gut and prevents malaria parasites in rodents from reproducing. The Johns Hopkins team put the transgenic and natural mosquitoes in cages with malaria-infected mice, on which the mosquitoes fed. Over time the mosquitoes reproduced. After nine generations, transgenic bugs made up 70 percent of the overall population. The disease-resistant strains not only competed with the wild ones but survived better.

Mosquitoes can be genetically engineered to avoid passing malaria to humans.

The test did not prove that infection-resistance genes would spread in the wild, but it raised hope that mosquitoes doped with those genes would survive. Hardly a month later, however, biologist Bruce A. Hay of the California Institute of Technology presented evidence that engineered genes can indeed spread throughout a bug population. Working with fruit flies, Hay's team combined a segment of noncoding RNA, known as a microRNA, with a gene that was critical to the development of fruit fly embryos; the researchers then altered that gene so that it was unaffected by the RNA. Next they released the fruit flies into cages with three times as many normal flies. As generations mixed, wild flies that incorporated the microRNA died because it destroyed their unprotected version of the critical developmental gene, whereas flies that bore the altered version of that gene were able to survive. After nine to 11 generations, all the offspring in the cage carried the human-made gene combination. —*Mark Fischetti*

FROM "BEATING THE STANDARD QUANTUM LIMIT WITH FOUR-ENTANGLED PHOTONS," BY T. NAGATA ET AL., IN *SCIENCE*, VOL. 316; 2007. REPRINTED WITH PERMISSION OF AAAS (*top*); SINCLAIR STAMMERS *Photo Researchers, Inc.* (*bottom*)

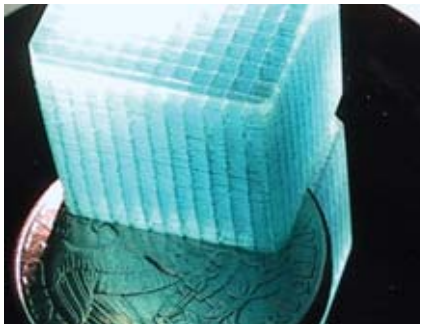
Material World

Scientists take inspiration from nature and instill novel magnetic properties

Cut your finger, and your body starts mending the wound even before you have had time to go and find a Band-Aid. Synthetic materials are not so forgiving, but Nancy R. Sottos, Scott R. White and their colleagues at the University of Illinois at Urbana-Champaign are looking to change all that. They developed a self-healing plastic that contains a three-dimensional network of microscopic capillaries filled with a liquid healing agent. When the material is cracked, the released fluid is hardened by particles of a catalyst that are also sprinkled throughout. The new material can repair minor cracks up to seven times at each location, improving on the group's previous system (in which the fluid was located in individual pockets) that could repair only one injury at each place.

Another feature of natural organisms that scientists have been seeking to emulate is self-assembly. Benoît Roman and José Bico of the City of Paris Industrial Physics and Chemistry Higher Education Institution used the surface tension of evaporating water droplets to fold flea-size origami cubes, pyramids and other structures. Their work used shapes measuring about a millimeter across cut out of a rubbery polymer a mere 40 to 80 microns thick. Thanks to the way that surface tension scales with size, the technique may be effective for self-assembling micron- or nanometer-scale objects made of thinner sheets of polymer.

Electronic components based on plastic or organic materials have become increasingly common in recent years, but the same cannot be said for magnets. Now Robin G. Hicks of the University of Victoria in British Columbia, Rajsapan Jain of the University of Windsor in Ontario and their co-workers have produced a new class of magnets that combine nickel with a variety of organic compounds. The dark, powdery substances remain magnetized up to 200 degrees Celsius. The researchers' ultimate goal is to produce magnetic organic compounds that can be easily molded into thin films or other useful shapes for electronics.



When cracked, the plastic cube releases a self-healing agent from its microvascular network—up to seven times at one location.

It was thought that the only way to see the exotic state of matter known as a Bose-Einstein condensate—in which a collection of particles essentially behaves as one superparticle—involved forbidding, near-absolute-zero cold. Sergej Demokritov of the University of Muenster in Germany and his colleagues were the first to create such condensates at room temperature. Demokritov used small, ephemeral packets of magnetic energy known as magnons, which he generated in yttrium-iron-garnet films by exposing them to microwaves. Magnons are far less massive than atoms and thus can form condensates at much higher temperatures.

—Graham P. Collins and Charles Q. Choi

Neurological Insights

Biologists devise a memory on a chip and new ways to tackle Alzheimer's

How does a memory form? To demonstrate how this process occurs at the most basic level, biophysicists at Tel Aviv University replicated that event with neurons attached to a computer chip. Itay Baruchi and Eshel Ben-Jacob placed neurons from rat embryos on a chip surface and connected 64 electrodes to record activity. The researchers witnessed an identical pattern of nerve firings when chemical stimulants were dropped repeatedly at the same location on the chip. After some time, the neurons began to fire in the same way without chemical activation—the point at which they claim a memory becomes imprinted.

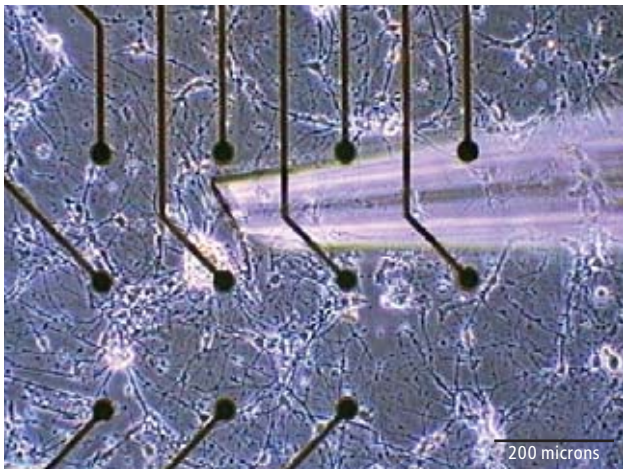
Understanding differences between the proteins made by normal and diseased brain tissues may provide a new approach to diagnostics. Richard D. Smith of the Pacific Northwest National Laboratory and Desmond J. Smith of the University of California, Los Angeles, have created a complex system for analyzing proteins that combines advanced instrumentation with sophisticated image processing to inspect one-millimeter cubes of brain tissue from a pair of normal mice. The investigators determined the abundance of 1,028 proteins in the tissues. Future experiments will use this methodology to compare normal brain tissue with that afflicted by a neurodegenerative disease.

Better diagnostic techniques are needed, in particular, for Alzheimer's disease.

ROB SHEPHERD *University of Illinois at Urbana-Champaign*

Stina M. Tucker, Esther Oh and Juan C. Troncoso of the Johns Hopkins University School of Medicine demonstrated a test using antibodies that bind to the amyloid-beta proteins that form damaging plaques in the brains of Alzheimer's patients. The antibodies adhered to proteins in an early stage of a disease that mimics Alzheimer's in genetically engineered mice. That finding might eventually lead to a test for humans that could be used along with drugs under development to avert the disease through preventive treatment.

Conceivably, that test could be combined with a treatment that uses phages—viruses that infect bacteria—to break up noxious plaque. Beka Solomon of Tel Aviv University showed preliminary proof of this idea by administering phages via a nasal spray to 100 mice genetically engineered to develop Alzheimer's-like plaques. After a year of treatment, the mice had 80 percent fewer plaques than untreated mice. —*Gary Stix*

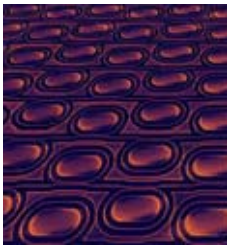


Electrodes record when neurons fire so that a memory forms.

Light Manipulation

New technologies exercise extraordinary control over light

As computer chips become ever more prodigious in their data-processing capacities, the task of shuttling all those gigabits around inside a chip becomes an increasing challenge. Help may be on the way in the form of photonic components, which deal in pulses of light instead of slower packets of electric charge. For several years researchers have been making so-called silicon optical waveguides, in which light speeds along inside the ridge between two channels as if along an optical fiber.



Microscopic loops control light pulses.

But such optical interconnects must deliver their data at precise times, which requires delaying the light pulses by controlled amounts. One method is to send the light pulses into microscopic loops made of waveguides where they circulate dozens of times before continuing on their journey. Yurii A. Vlasov and his coworkers at the IBM Thomas J. Watson Research Center in Yorktown Heights, N.Y., sent pulses of light through strings of as many as 100 such loops without suffering prohibitive losses of data.

Another way of delaying light in microscopic devices is to use photonic crystal components, which contain carefully designed arrays of holes whose size and spacing exclude light in a certain frequency band (a so-called photonic band gap). A photonic crystal waveguide can consist of a path without holes running through such an array in a thin slab of silicon. The band gap generated by the holes on each side of the path confines the light to travel that route. Takasumi Tanabe and his colleagues at the NTT Basic Research Laboratories in Japan took this scheme several steps forward by temporarily storing photons in a photonic crystal nanocavity—in this case, a small region where the waveguide is slightly wider.

Whereas some researchers want to delay light, others at the Rensselaer Polytechnic Institute led by E. Fred Schubert have created a coating that reflects almost none of it. The coating, about 600 nanometers thick, consisted of five layers of nanorods—titanium dioxide and silica filaments about 25 nanometers in diameter and up to 300 nanometers long—stacked on a transparent semiconductor wafer. Each layer had a lower refractive index than the one below it. The uncoated semiconductor reflected about 12 percent of light incident on it; when coated, it reflected as little as 0.1 percent. The coating could have applications in photonic components, light-emitting diodes and solar cells.

Other investigators are pursuing the far more speculative goal of building quantum computers, which would exploit weird features of quantum mechanics to achieve unprecedented processing capabilities. One approach involves storing quantum data as long-lived states of atoms and transmitting the information with light waves. But combining those two media requires the transfer of delicate quantum states between matter and light. In 2006 a group of researchers led by experimentalist Eugene S. Polzik of the Niels Bohr Institute at the University of Copenhagen and theorist Ignacio Cirac of the Max Planck Institute for Quantum Optics in Garching, Germany, teleported quantum information from a light pulse to a cloud of atoms. —*Graham P. Collins*

ITAY BARUCHI AND ESHEL BEN-JACOB (*top*); IBM (*bottom*)

Progress against Prions

Ideas for treating the human form of mad cow disease begin to emerge

More than 200 cases of variant Creutzfeldt-Jakob disease, the human form of mad cow, have occurred worldwide since the 1990s. No accepted treatment exists for the devastatingly fatal disease or any of the others caused by infection with the malformed, malignant protein particles called prions. Giovanna R. Mallucci and her co-workers at the Institute of Neurology in London have performed an experiment in mice that could lay the groundwork for an eventual cure. Researchers genetically engineered mice to produce the protein PrP for only the first nine weeks after birth. PrP misfolds in the presence of prions, which causes it to produce more prions.

When both the altered mice and a normal group were injected with prions causing the illness called scrapie, both groups experienced a cognitive decline at first. The normal subjects continued to deteriorate. But by 12 weeks, the engineered group, without an ongoing supply of PrP, had recovered memory and normal behavior patterns. The absence of the natural protein did not appear to have an adverse effect on the restored rodents. If this approach proves itself further, it might lead to drugs or gene therapies that diminish PrP.

Blood filters through beads coated with a compound that readily sticks to prions.

Until that happens, the possibility of prions infecting people through the blood supply remains an ever present fear. Robert Rohwer of the Veterans Affairs Medical Center in Baltimore and his colleagues invented a filter that might be able to purge red blood cells of prions. The team members began by searching through a library of millions of chemicals until they discovered a compound, L13, that readily sticks to prions. Scrapie-containing blood filtered through beads coated with L13 and then injected into hamsters did not cause disease in the animals, unlike tainted, unfiltered blood.

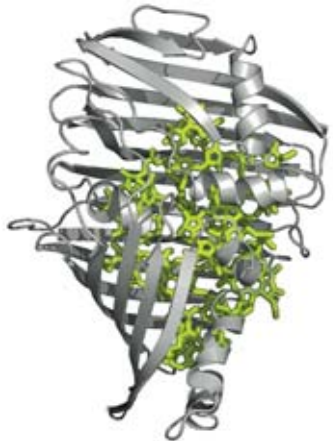
—*Gary Stix*

Sun Power Gets a Boost

A stolen idea from the plant world could improve prospects for solar power

Photovoltaic cells can generate electricity without adding greenhouse gases to the atmosphere, but solar power is significantly more expensive than the electricity produced by coal- and gas-fired plants. To boost the competitiveness of solar energy, researchers have striven to make solar cells convert sunlight into electricity more efficiently.

Inspiration may come from the most basic scientific research. Investigators are starting to delve into the intricacies of photosynthesis, which converts sunlight into chemical energy with almost 100 percent efficiency. A group led by Gregory S. Engel, formerly at the University of California, Berkeley, and now at the University of Chicago, cooled a green sulfur bacterium to 77 kelvins (–321 degrees Fahrenheit) and then zapped it with ultrashort pulses from a laser, enabling the tracking of the energy flow through the bacterium's photosynthetic apparatus.



Insights into the photosynthesis system for bacteria (*above*) and other organisms may improve solar technology.

The researchers found that by using this spectroscopy technique, they could explain how plants efficiently transfer solar energy to molecular reaction centers for conversion into chemical energy. The previous view of photosynthesis postulated that light-harvesting molecules called chromophores absorbed energy from the sun and then transferred it from one such molecule to another along one of various possible routes until reaching a reaction center.

The study found that in contrast to the prevailing notion, energy moves in a wavelike motion along all the pathways in the system at once, a quantum effect that ensures that the energy takes the most efficient route, arriving at its destination almost instantaneously. Eventually this new understanding may become the basis for an artificial photosynthesis process that can be incor-

MACOPHARMA (*top*); GREG ENGEL (*bottom*)

porated into the design of more efficient photovoltaic cells.

Other scientists are devising better ways to use sunlight to heat and cool buildings. Steven Van Dessel of the Rensselaer Polytechnic Institute and his colleagues have developed a prototype system called the Active Building Envelope (ABE), which couples solar panels to thermoelectric heat pumps. Electricity produced by the solar cells goes to the heat pumps, which can either heat or cool the building's interior, depending on the direction of the flow of the current. The research group is now investigating the possibility of creating a transparent ABE system using thin-film photovoltaic cells and thermoelectric materials instead of bulky components. The transparent films could be applied like a glaze to the windows of buildings and to the windshields and sunroofs of cars. —*Mark Alpert*

Stem Cell Control

The essential character of the mother of all cells reveals itself in a set of breakthrough findings

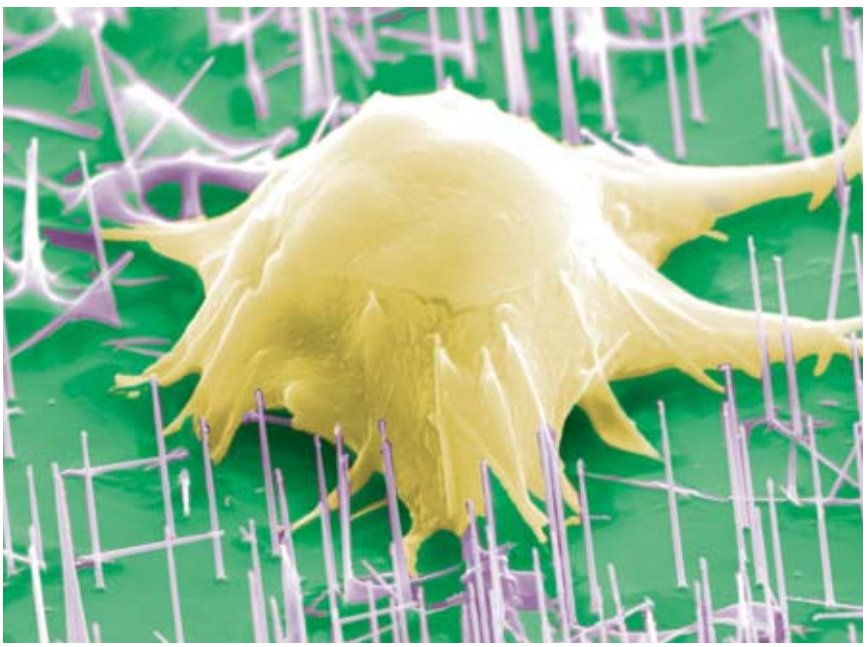
The all-powerful potential of stem cells to become any kind of cell is what makes them so promising for restoring diseased or damaged tissues throughout the body—and also what makes them so difficult for scientists to control. But several breakthroughs represent major strides toward understanding and harnessing the cells' elusive property of inherent "stemness."

Shinya Yamanaka of Kyoto University, who transformed a regular mouse skin cell into a cell with most of the characteristics of embryonic stem cells (ESCs) by turning up the activity of just four genes, demonstrated recently a more precise way of isolating cells "reprogrammed" to an ESC-like state—and several other laboratories have replicated his results.

Coaxing cultured ESCs to go in the opposite direction—to become skin cells or some other type of tissue—is a tricky process involving the cells' own gene activity and signals from their surrounding environment. Peidong Yang of the University of California, Berkeley, and Bruce R. Conklin of the Gladstone Institute of Cardiovascular Disease in San Francisco showed a new way to deliver those external signals by growing ESCs embedded with nanoscale silicon wires. Yang and Conklin envision the technique being used to guide the differentiation of stem cells into specific tissue types through electrical pulses or chemicals transmitted via nanowires.

As some researchers worked on controlling the differentiation of ESCs, others were focused on finding out what keeps adult stem cells in an undifferentiated state. Frank D. McKeon of Harvard Medical School showed last year that the activity of a single gene, known as *p63*, is the key to a cell staying a stem, at least in epithelial cell types, which include a variety of tissues such as skin, prostate, breast and thymus.

There is no shortage of adult stem cells for investigators who want to probe their relation to health and disease, but that is not true for ESC scientists who typically must first create embryos from hard-to-procure eggs. A technique for recycling unhealthy fertilized embryos, which have no other viable use, has promise as a source of ESCs for research. Kevin Eggan of the Harvard Stem Cell Institute and his team used aberrant embryos with extra chromosome sets—which can occur naturally during in vitro embryo creation when two sperm fertilize an egg—as stand-ins for the precious eggs. They found that when the chromosomes were removed and new genetic material introduced, the resulting embryo developed successfully about as often as embryos made from eggs and yielded stem cells that were apparently normal. —*Christine Soares*



Nanowires could deliver signals to prompt a stem cell to differentiate into another cell type.

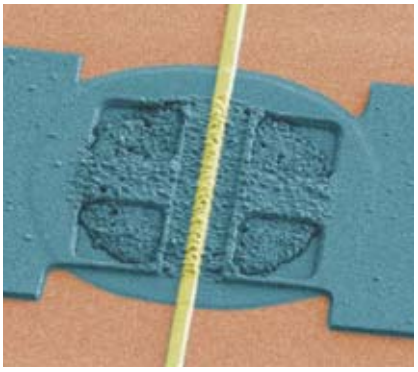
PEIDONG YANG *University of California, Berkeley*

Squirt and Spin

Printers squirt out silicon chips, and the spin of electrons is used in computer logic

We now look back with pity on old computer printers, with their glacial bizz-buzz and annoying perforated-edge paper. A decade from now people will surely look back in pity on the things we call printers today. Three-dimensional printers, capable of producing entire objects, are already coming down in price, and new types of printers can output electronic circuit boards or even entire functional circuits. Now researchers have a printer that outputs silicon chips.

The device, created by materials scientist Masahiro Furusawa of Seiko Epson Corporation in Japan and his colleagues, squirts out polysilane, a polymer of silicon and hydrogen. Once laid down, it can be baked at kitchen-oven-cleaning temperatures to drive out the hydrogen and leave behind crystalline silicon. The technique provides an alternative to the conventional process for producing microchips, which requires refining, stenciling and etching the silicon—a sequence that is both complicated and wasteful: 99 percent of the original silicon is thrown away. The silicon printer is still fussy and does not produce chips with as fine a level of detail. Nevertheless, it might lower the cost of low-resolution silicon devices such as display circuitry and solar cells.



Transistor made from polysilicon was literally printed onto a surface.

Gizmo users of the future will also look back in pity on what flows through those circuits. Right now circuits convey signals by the presence or absence of electrons, ignoring the particles' spin (the quantum analogue of rotation). The emerging technology of spin-based electronics, or "spintronics," seeks to make use of this wasted information. So far its only application has been in hard disks. Researchers have also sought to exploit it in logic gates for computational processing, not least because it takes less energy to flip an electron's spin than to change its direction of motion. The hang-up is that detecting and manipulating spin requires magnets, which are tricky to integrate into silicon circuits.

Physicist Hanan Dery of the University of California, San Diego, and his colleagues have now come up with a workable logic-gate design. A combination of fixed magnets and voltage levels steers electrons based on their spin and the desired gate function. The team outlined a proposal for a spintronics computer based on the gate, but it remains to be seen whether it will work in practice.

—*George Musser*

Making Them Whole

Artificial limbs and a prosthetic arm create a path to better bionics

Research on prosthetics takes its greatest strides during or just after wartime, and the past several years have sadly been no exception. Todd A. Kuiken of the Rehabilitation Institute of Chicago and his team have pioneered "targeted reinnervation," which jacks an artificial arm into the nervous system. They transplant nerves from the shoulder of a lost arm to a patch on the chest. In trying to move the arm, the person causes chest muscles to flex, which electrodes pick up and transmit to the prosthesis. The researchers have begun to experiment with two-way connections, relaying signals from sensors on the arm to sensory nerves.

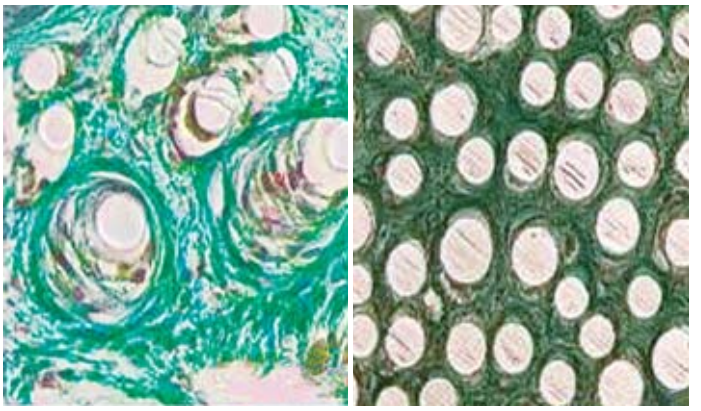
Details about the prosthetic arm by Segway inventor Dean Kamen of DEKA Research & Development Corporation are limited to a YouTube video (www.youtube.com/watch?v=1hzRja9eunY), but it is jaw-dropping. In a demonstration that looks like a scene from *Bionic Woman*, an engineer wearing

Patient at the Rehabilitation Institute of Chicago demonstrates the manual control that can be achieved with one of his protheses.

a prototype arm grasps a water bottle, picks up a pen and scratches his nose. One can only hope that, unlike the Segway, it will be priced at a level affordable to all.

Every year more than 200,000 Americans tear their knee ligaments, which, as the Mafia knows, is a painful and hard-to-treat injury. Cato T. Laurencin of the University of Virginia and his team have developed polymers that serve as tissue scaffolding, promoting the growth of brand-new ligaments. In tests on rabbits' knees, the regenerated ligament supported a third as much tension as a fresh one. To be sure, half the bunnies suffered new ruptures, but Laurencin attributed this to the difficulty of convincing them to go through physical therapy.

—*George Musser*



Polymer fibers (*shown in cross section*) encourage growth of new ligaments.

The Fastest Way to Get There

Novel ways of calculating routes and predicting traffic jams promise less time in the car

Providing directions instantly online has until recently meant that navigational mapping programs, such as MapQuest and Google Maps, often simplify the problem by not considering every possible route to a destination. Scientists at the University of Karlsruhe in Germany have designed a computer application that can quickly calculate the most expedient of all possible driving routes without the need for excessive computation.

Dominik Schultes, one of the project's scientists, designed the program around a simple premise: driving somewhere usually requires crossing major intersections that are sparsely interconnected. Figuring the best route occurs by precomputing the connections between a starting point (or destination) and its nearest major intersections and between all locations where major routes cross each other's paths—so-called transit nodes. When this parsimonious algorithm was tested on densely routed maps of western Europe and the U.S., the route calculations improved by a factor of 100.

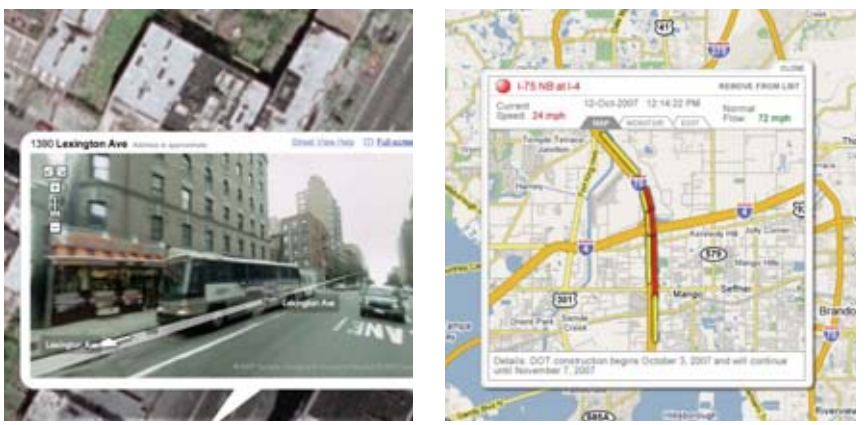
To actually ensure that drivers do not go astray on their road excursion, Google has begun installing an option to its mapping program that provides a street-level navigational view. With a system of successive panoramic snapshots of the suggested route, Google Street View allows travelers to verify the landmarks they will encounter from the driver's seat.

Even with the best directions in hand, unforeseeable traffic can ruin a trip. IntelliOne, a company that explores ways to combine transportation and communications networks, has recently unveiled the TrafficAid, which translates anonymous cell phone signals into an accurate, real-time traffic map.

By harnessing ubiquitous cellular networks, the system avoids having to install separate sensors along traffic routes. Specific servers, instead, can detect a phone's specific location and speed. IntelliOne transfers these signaling data to its database, where detected phones are associated with a certain road, thereby producing accurate and timely information about traffic conditions.

Freed of dependence on traffic information from video cameras, roadside radars and in-pavement monitors, the TrafficAid updates its map of bunched signals more quickly and makes a calculation to within five to eight kilometers (three to five miles) per hour of actual speed.

—*Peter Sergo*



Street View (*left*) adds imagery of U.S. cities to Google's mapping program, whereas TrafficAid (*right*) transforms signals received from cell phones into a real-time traffic map.

See-Through Technology and Better Sleep

A mix of technology accompanies the doings of a maverick researcher

T-ray Vision

In principle, terahertz radiation—which lies between the microwave and infrared segments of the electromagnetic spectrum—could help people safely peer through flesh, plastic, fabrics and ceramics to detect anomalies, from tumors to bombs, for medical or security applications. But for decades, so-called t-ray devices were impractical outside the lab because they were fragile and because they weighed 45 kilograms (100 pounds) or more. Yet after just a few months of work, Brian Schulkin of the Rensselaer Polytechnic Institute created a rugged t-ray imager dubbed the "Mini-Z" that is less than 2.3 kilograms (five pounds) in weight and can fit in a briefcase. A prototype detected flaws purposely embedded in samples of foam used to insulate the space shuttle. Schulkin next plans to develop a handheld t-ray device. —*Charles Q. Choi*

Load-Lightening Backpack

A few hardcover textbooks in a school backpack are enough to cause muscle strain. Lawrence C. Rome of the University of Pennsylvania and of the Marine Biological Laboratory in Woods Hole, Mass., and his colleagues have developed a backpack suspension system that minimizes stress on its wearer. As people walk, they typically bob up and down by several centimeters, which causes a pack to swing up and down. A 2.3-kilogram (five-pound) laptop slams down with 3.7 kilograms (eight pounds) of force when walking and as much as 6.9 kilograms (15 pounds) when running. Using pulleys and bungee cords, the new backpack damps this motion by half or more. In effect, the pack feels about a fifth lighter.

One version even generates electricity—more than seven watts, enough to recharge phones. Rome has set up a company, Lightning Packs, to develop the idea. —*George Musser*

Better Sleep Aid

About nine years ago researchers discovered that the sudden spells of sleepiness called narcolepsy were caused by a deficit of a brain peptide called orexin. Actelion Pharmaceuticals in Allschwil, Switzerland, used this knowledge to create a type of sleeping pill that works by blocking two orexin receptors. Drug tests have shown that the compound known as ACT-078573 induces sleep in both animals and humans. —*Gary Stix*

Antiparasite Weapon

The debilitating parasitic illness known as schistosomiasis infects roughly 200 million people worldwide, making it second only to malaria in importance for public health. Currently just one drug, praziquantel, commonly treats the chronic disease, raising fears that the parasite could evolve resistance against it. Now Conor R. Caffrey of the University of California, San Francisco, and his colleagues have found a new drug that can kill the blood flukes that cause the ailment. They investigated the drug K11777, which interferes with the flukes' digestive enzymes, and discovered that it could eliminate the parasites in lab mice.

If effective in humans, K11777 could work in tandem with praziquantel, with the former taking care of early-stage illnesses and the latter killing later-stage infections. —*Charles Q. Choi*

A new drug may fight the parasites that cause schistosomiasis.

Bird Flu Research for All

Until recently, laboratories doing bird flu research often kept their findings private, with access to many avian influenza gene sequences confined to just 15 facilities globally, potentially hindering them from doing research that could provide new insight into the virus. Instead of entering her avian influenza findings into this database, Ilaria Capua of Vialle University in Padua, Italy, disclosed the results of her studies in the publicly accessible GenBank and boldly rallied her colleagues to follow.

Her efforts helped to pave the way for the Global Initiative on Sharing Avian Influenza Data, a consortium through which findings can be freely shared while giving credit to researchers involved. —*Charles Q. Choi*

Peer-through technology has gone mobile.

BRIAN SCHULKIN (*left*); NATIONAL CANCER INSTITUTE/PHOTO RESEARCHERS, INC. (*right*)

Research Leader of the Year

1. The Wellcome Trust Case Control Consortium

Business Leader of the Year

2. Amyris Biotechnologies

Policy Leader of the Year

3. X Prize Foundation

Other Research, Business and Policy Leaders

Connections to an Untethered Future

4. Marin Soljačić, Massachusetts Institute of Technology (research)
5. Apple (business)
6. Robert Ghrist, University of Illinois at Urbana-Champaign, and Vin de Silva, Pomona College (research)

Getting from Here to There

7. Manjunath N. Swamy, Immune Disease Institute, Harvard Medical School (research)
8. Hans Boumans, Netherlands Organization for Applied Research (research)

Fueling Alternatives

9. James A. Dumesic, University of Wisconsin–Madison (research)
10. Radoslav R. Adzic, Brookhaven National Laboratory (research)
11. Shelley D. Minteer and Tamara Klotzbach, Saint Louis University (research)

Fighting Toxins in the Home

12. Patricia A. Hunt, Washington State University (research)
13. American Pharmacists Association and the U.S. Fish and Wildlife Service (policy)

Advances in Ultrameasurement

14. Peter W. Sutter and Eli A. Sutter, Brookhaven National Laboratory (research)
15. Groups of physicists at Hokkaido University, Japan, and the University of Bristol, England (research)

Mosquitoes Enlisted to Beat Malaria

16. Marcelo Jacobs-Lorena, Johns Hopkins University (research)
17. Bruce A. Hay, California Institute of Technology (research)

Material World

18. Nancy R. Sottos and Scott R. White, University of Illinois at Urbana-Champaign (research)
19. Benoît Roman and José Bico, City of Paris Industrial Physics and Chemistry Higher Education Institution (research)
20. Robin G. Hicks, University of Victoria, British Columbia, and Rajsapan Jain, University of Windsor, Ontario (research)
21. Sergej Demokritov, University of Muenster, Germany (research)

Neurological Insights

22. Itay Baruchi and Eshel Ben-Jacob, Tel Aviv University (research)
23. Richard D. Smith, Pacific Northwest National Laboratory, and Desmond J. Smith, University of California, Los Angeles (research)
24. Stina M. Tucker, Esther Oh and Juan C. Troncoso, Johns Hopkins University School of Medicine (research)
25. Beka Solomon, Tel Aviv University (research)

Light Manipulation

26. Yurii A. Vlasov, IBM Thomas J. Watson Research Center (research)
27. Takasumi Tanabe, NTT Basic Research Laboratories, Japan (research)
28. E. Fred Schubert, Rensselaer Polytechnic Institute (research)
29. Eugene S. Polzik, Niels Bohr Institute, University of Copenhagen, and Ignacio Cirac, Max Planck Institute for Quantum Optics, Germany (research)

Progress against Prions

30. Giovanna R. Mallucci, Institute of Neurology, London (research)
31. Robert Rohwer, Veterans Affairs Medical Center, Baltimore (research)

Sun Power Gets a Boost

32. Gregory S. Engel, University of Chicago (research)
33. Steven Van Dessel, Rensselaer Polytechnic Institute (research)

Stem Cell Control

34. Shinya Yamanaka, Kyoto University (research)
35. Peidong Yang, University of California, Berkeley, and Bruce R. Conklin, Gladstone Institute of Cardiovascular Disease, San Francisco (research)
36. Frank D. McKeon, Harvard Medical School (research)
37. Kevin Eggan, Harvard Stem Cell Institute (research)

Squirt and Spin

38. Masahiro Furusawa, Seiko Epson Corporation, Japan (business)
39. Hanan Dery, University of California, San Diego (research)

Making Them Whole

40. Todd A. Kuiken, Rehabilitation Institute of Chicago (research)
41. Dean Kamen, DEKA Research & Development Corporation (research)
42. Cato T. Laurencin, University of Virginia (research)

The Fastest Way to Get There

43. Dominik Schultes, University of Karlsruhe, Germany (research)
44. Google (business)
45. IntelliOne (business)

See-Through Technology and Better Sleep

46. Brian Schulkin, Rensselaer Polytechnic Institute (research)
47. Lawrence C. Rome, University of Pennsylvania and Marine Biological Laboratory, Woods Hole, Mass. (research)
48. Actelion Pharmaceuticals, Switzerland (business)
49. Conor R. Caffrey, University of California, San Francisco (research)
50. Ilaria Capua, Vialle University, Italy (policy)

SCIENTIFIC AMERICAN

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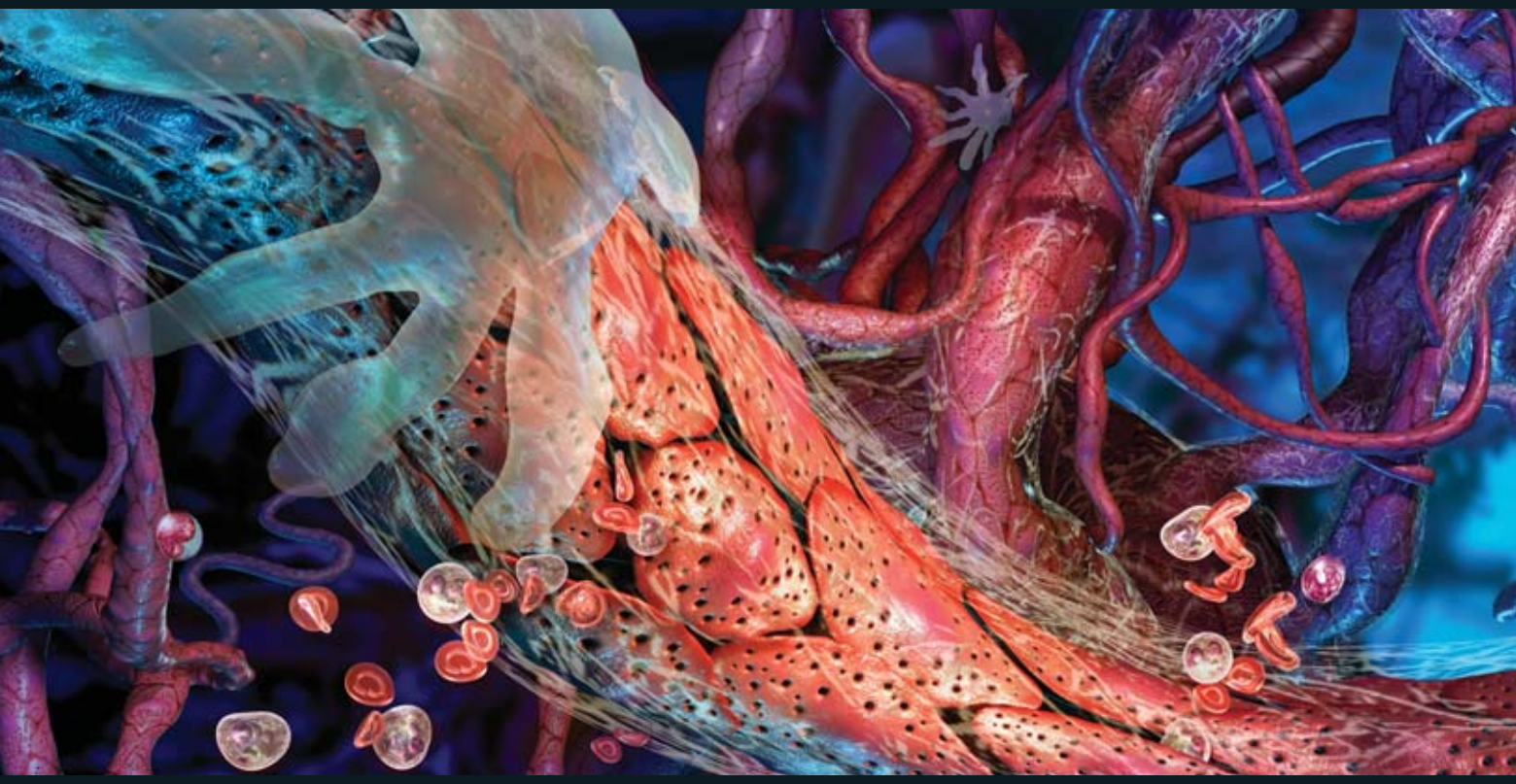
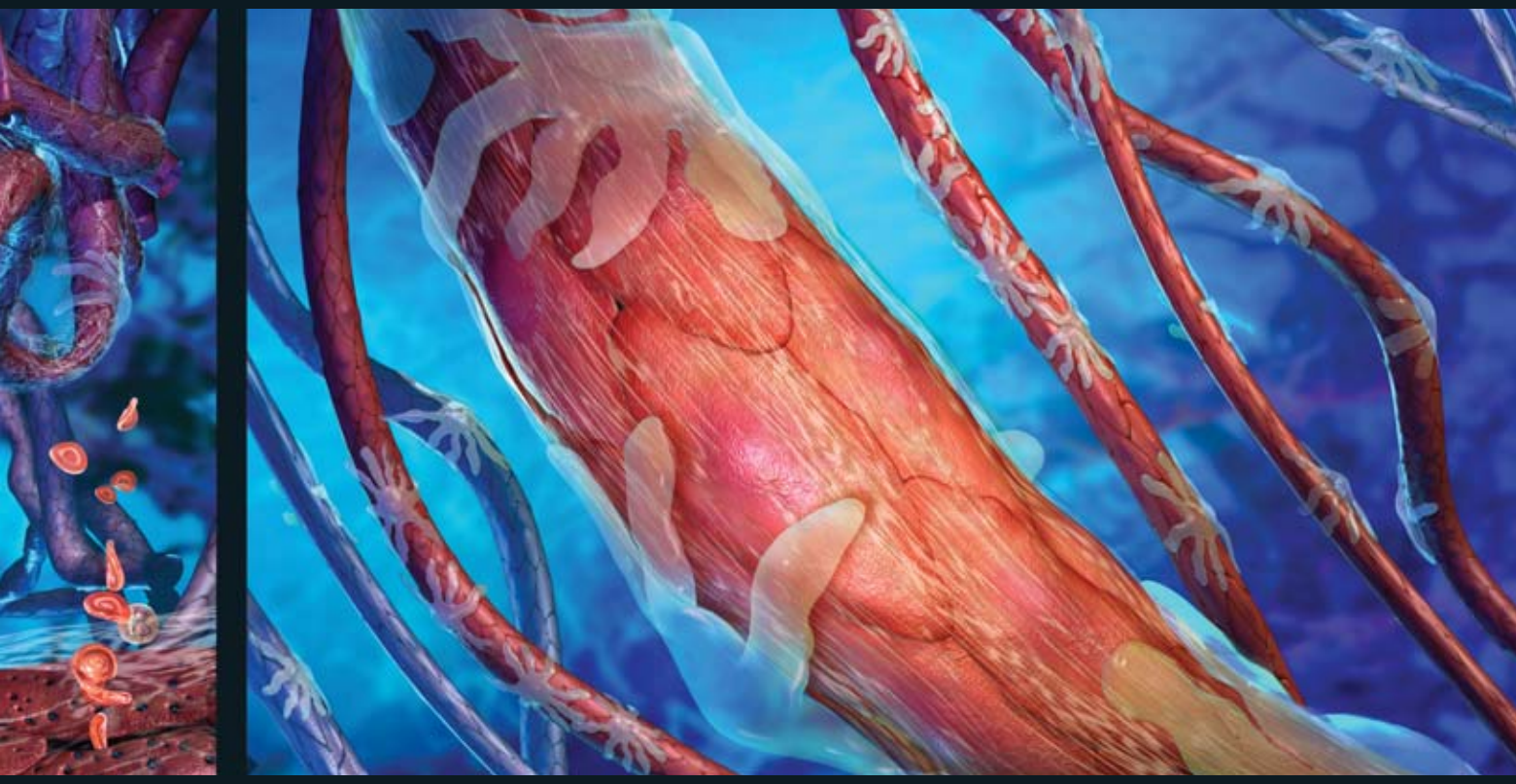


TAMING VESSELS TO TREAT CANCER

Restoring order to the chaotic blood vessels inside a tumor opens a window of opportunity for attacking it. Surprisingly, drugs meant to destroy vasculature can make the repairs and may help reverse conditions that lead to cardiovascular disease and blindness

By Rakesh K. Jain

While still a graduate student in 1974, I had a chance to see malignant tumors from a most unusual perspective. I was working at the National Cancer Institute in the laboratory of the late Pietro M. Gullino, who had developed an innovative experimental setup for studying cancer biology—a tumor mass that was connected to the circulatory system of a rat by just a single artery and a single vein. As a chemical engineer, I decided to use this opportunity to measure how much of a drug injected into the animal would flow to the tumor and back out again. Amazingly, most of the substance injected into the rat never entered the tumor. To make matters



ABNORMAL BLOOD VESSELS (*left*) add to the havoc inside a tumor and prevent treatments from reaching cancer cells. Normalizing those vessels (*above*) makes them into functional weapons that can be turned against the tumor.

KEITH KASNOT

worse, the small amount that did reach the mass was distributed unevenly, with some areas accumulating hardly any drug at all.

My immediate concern was that even if a small fraction of the cancer cells in a human tumor did not receive an adequate dose of whatever anticancer drug was being applied, those cells could survive—causing the tumor to grow back sooner or later. Perhaps the engineer in me was also drawn to trying to understand and solve the apparent infrastructure problem inside tumors that posed a major obstacle to the delivery of cancer therapies.

Over the subsequent decades my colleagues and I have investigated what makes the vasculature within tumors abnormal and how these disordered blood vessels not only stymie traditional cancer treatments but also contribute directly to some of the malignant properties of solid cancers. Building on these insights, we developed approaches to normalizing tumor blood vessels and tested them successfully in mice. In the process, we also discovered a seeming paradox—a class of drugs designed to destroy the blood vessels of tumors actually acts to repair them, creating a window of opportunity to attack the cancer most effectively.

In recent years we have finally been able to start testing this idea in cancer patients, and the excitement in our lab was overwhelming when we saw the first clinical evidence of tumors shrinking in response to vascular normalization, just as we had anticipated. Much more work remains before we can perfect this therapeutic approach and gauge its usefulness in patients with different types of malignancy. But what we have already learned about restoring blood vessels is also opening doors to treating other vascular disorders, such as macular degeneration, the leading cause of blindness in the U.S.

Tortuous Road

The journey that led to our recent successes began in earnest a few years after I completed my doctoral studies. Determined to find out why drugs do not penetrate tumors uniformly, my colleagues and I started by monitoring every step of the process in rodents. Using a variety of techniques, we observed the progress of drugs as they entered the tiny blood vessels of a tumor, crossed

KEY CONCEPTS

- Abnormal and dysfunctional blood vessels are a hallmark of solid tumors, one that contributes directly to malignant properties of a cancer as well as preventing treatments from reaching and attacking tumor cells.
- Normalizing tumor vessels allows cancer therapies to penetrate the mass and to function more effectively.
- Unexpectedly, drugs originally designed to destroy tumor blood vessels act to repair them for a time, opening a new avenue for cancer treatment as well as restoration of abnormal vasculature in other diseases. *—The Editors*

the vessel walls into the surrounding tissue, entered into cancer cells and eventually exited the mass. Together with my students and collaborators, we developed methods for tracking molecules, such as oxygen, within blood vessels and tissues. Eventually we could even watch as genes turned on and off inside cells.

Early on it was apparent that the vessels within tumors bear little resemblance to normal ones. Healthy tissues are fed by straight vessels that branch predictably into successively smaller capillaries and microvessels, creating a pervasive network for delivering oxygen and nutrients to cells. Tumors, which stimulate the growth of new vasculature of their own, tend to generate a tangle of vessels. These connect to one another randomly, with some oversize branches, many extraneous immature microvessels and areas of a tumor that will lack vessels altogether.

Over the course of many years we managed to delineate the processes that govern the movement of fluids, drugs and cells within this tortuous vasculature and gained insight into the consequences of the abnormalities. The picture that emerged was grim: the very first thing we realized was that tumor blood vessels are not just disorganized in their appearance but highly aberrant in every aspect of their structure and function. We found that blood flows quite briskly in some vessels within a tumor, whereas it is static in others. In a given vessel, blood may travel in one direction for a while and then reverse direction. These flow patterns alone create a major obstacle to uniform drug delivery. Moreover, some parts of the vessel walls are overly leaky and others are unusually tight,

[THE PROBLEM]

ABNORMAL VESSELS MAKE TROUBLE

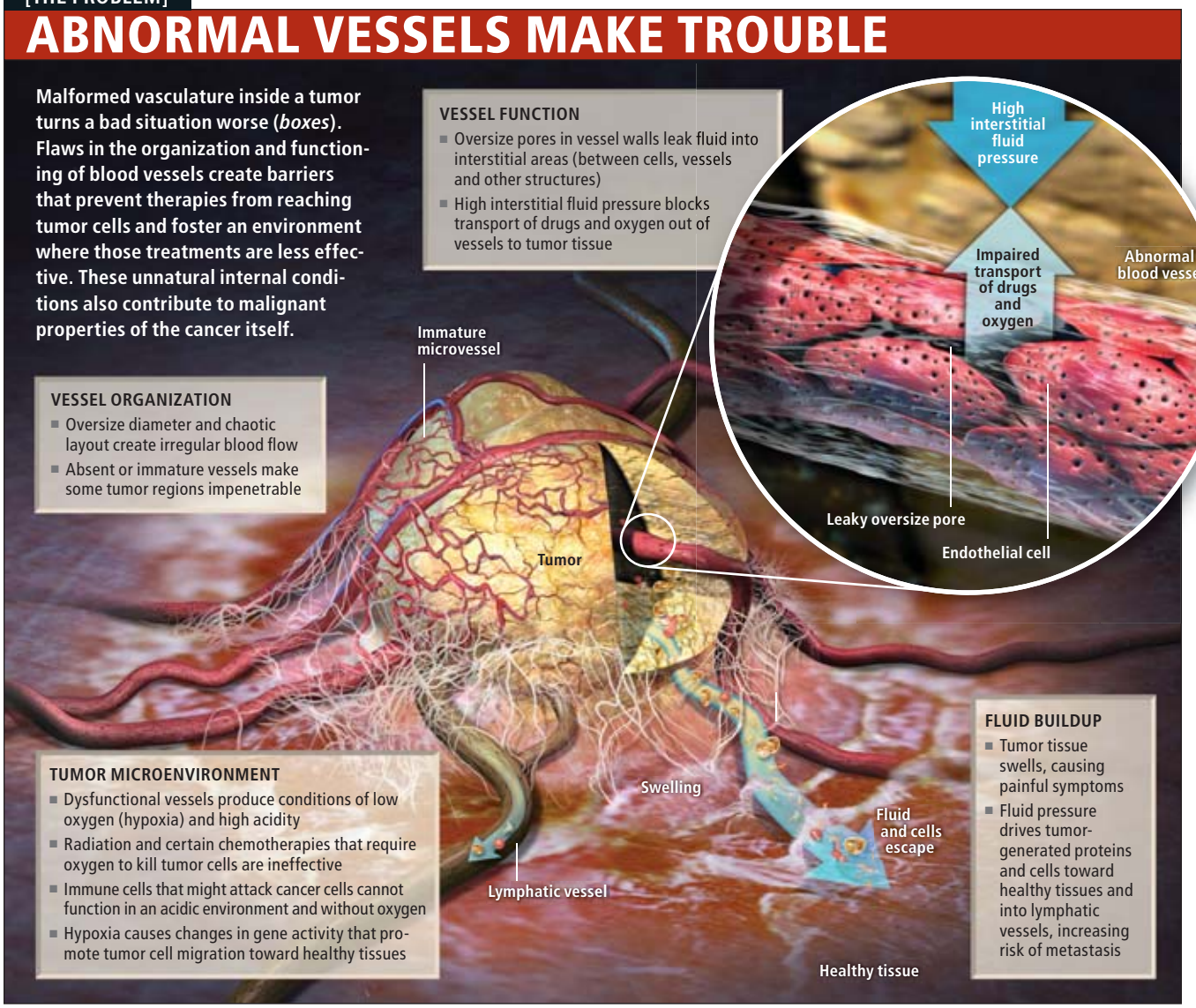
Malformed vasculature inside a tumor turns a bad situation worse (*boxes*). Flaws in the organization and functioning of blood vessels create barriers that prevent therapies from reaching tumor cells and foster an environment where those treatments are less effective. These unnatural internal conditions also contribute to malignant properties of the cancer itself.

VESSEL FUNCTION
- Oversize pores in vessel walls leak fluid into interstitial areas (between cells, vessels and other structures)
- High interstitial fluid pressure blocks transport of drugs and oxygen out of vessels to tumor tissue

VESSEL ORGANIZATION
- Oversize diameter and chaotic layout create irregular blood flow
- Absent or immature vessels make some tumor regions impenetrable

TUMOR MICROENVIRONMENT
- Dysfunctional vessels produce conditions of low oxygen (hypoxia) and high acidity
- Radiation and certain chemotherapies that require oxygen to kill tumor cells are ineffective
- Immune cells that might attack cancer cells cannot function in an acidic environment and without oxygen
- Hypoxia causes changes in gene activity that promote tumor cell migration toward healthy tissues

FLUID BUILDUP
- Tumor tissue swells, causing painful symptoms
- Fluid pressure drives tumor-generated proteins and cells toward healthy tissues and into lymphatic vessels, increasing risk of metastasis



KEITH KASNOT

which means that drugs and other molecules that managed to penetrate the vasculature would be distributed into the surrounding tumor tissue unevenly.

When we began investigating the causes of this nonuniform porousness, we discovered that in some tumors the pores in blood vessel walls could be as large as one or two microns in diameter, which is more than 100 times the size of pores in healthy vessels. As a result, these vessels are unable to maintain normal pressure gradients across their walls. Fluid pressure inside healthy blood vessels is typically much higher than in the surrounding tissue. Because tumor vessels are so porous, escaping fluid raises the outside—or interstitial—pressure until it nearly equals that inside the blood vessels.

This unnatural pressure gradient is not just an impediment to the ability of drugs to reach tumor cells; the accumulation of interstitial fluid produces swelling in and around tumor tissues. In patients with brain cancers, where tissue expansion is limited by the skull, that swelling becomes a severe, often life-threatening problem in itself. In those with other types of cancer, the exuded fluid can also accumulate in body cavities. Wherever it goes, the fluid oozing from a tumor carries with it tumor cells as well as various tumor-generated proteins that promote the growth of new blood and lymphatic vessels in the surrounding normal tissue and lymph nodes—which can then serve as conduits for the metastatic spread of the cancer cells to other parts of the body.

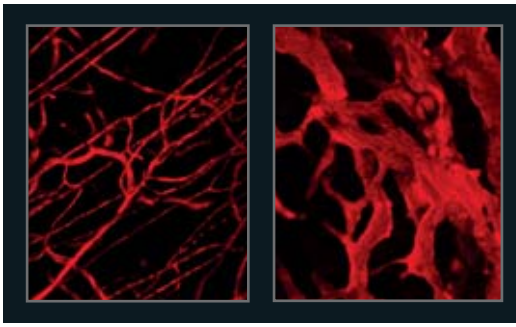
Beyond the difficulty of delivering drugs through chaotic tumor vasculature and the dangerous fluid buildup caused by leaky vascular walls, the abnormalities of tumor vessels create a highly unnatural microenvironment inside a tumor as well. Because many areas of a tumor lack vasculature and existing vessels are unable to deliver sufficient oxygen to surrounding tissues, a general state of hypoxia (low oxygen) and high acidity prevails in the tumor. Hypoxia in turn makes tumor cells more aggressive and prone to metastasis. In addition, the body's immune cells, which might help fight a tumor, are hampered by acidity and cannot function in low oxygen. Nor can radiation treatments and a subset of chemotherapy drugs that depend on chemical processes that require oxygen to kill cancer cells.

Thus, what began as an inquiry into seemingly simple aberrations in the flow of drugs inside tumors revealed that the abnormalities in tumor blood vessels are obstacles to treatment in even more ways than I had initially imagined. In 1994 I described our findings up to that point in-depth in this magazine [see "Barriers to Drug Delivery in Solid Tumors," by Rakesh K. Jain; Scientific American, July 1994]. By that time, these observations were also beginning to suggest to my research collaborators and me that if we knew how to repair the structure and function of tumor-associated blood vessels, we would have a chance to normalize the tumor microenvironment and ultimately improve cancer treatment. To accomplish such a reversal, we first had to gain a better understanding of what makes tumor vessels abnormal and keeps them that way.

Restoring Balance

We began to look at the molecular factors involved in normal blood vessel formation, known as angiogenesis, including the single most potent one, vascular endothelial growth factor (VEGF). First discovered and named vascular permeability factor by my Harvard University colleague Harold Dvorak, VEGF promotes the survival and proliferation of endothelial cells, which form the inner lining of blood vessels. In excess, it also makes vessels leaky—hence its original name. In normal tissues, however, the collective action of VEGF and other growth-stimulating molecules like it is counterbalanced by the actions of natural antiangiogenesis molecules, such as thrombospondin, that inhibit blood vessel growth.

Whether healthy or diseased, tissues that need new blood vessels increase their production of angiogenesis stimulators or reduce their production of inhibitors, or do both, tipping the balance in favor of angiogenesis. In healthy processes such as wound healing, a balance between growth and inhibitory factors is eventually reinstated once the new vessels are established. But in tumors and a number of other chronic diseases, an imbalance persists—and blood vessels grow increasingly abnormal.



BLOOD VESSELS in a normal mouse muscle's capillary bed (*far left*) and inside a mouse tumor (*left*) differ distinctly. The tumor vessels branch erratically, vary in diameter along their lengths and are generally oversize—all features that contribute to irregular blood flow.

LANCE L. MUNN *Harvard Medical School (Jain)*; FROM "MOLECULAR REGULATION OF VESSEL MATURATION," BY RAKESH K. JAIN, IN *NATURE MEDICINE*, VOL. 9; 2003. REPRINTED WITH PERMISSION FROM MACMILLAN PUBLISHERS LTD. (*micrographs*)

[THE AUTHOR]

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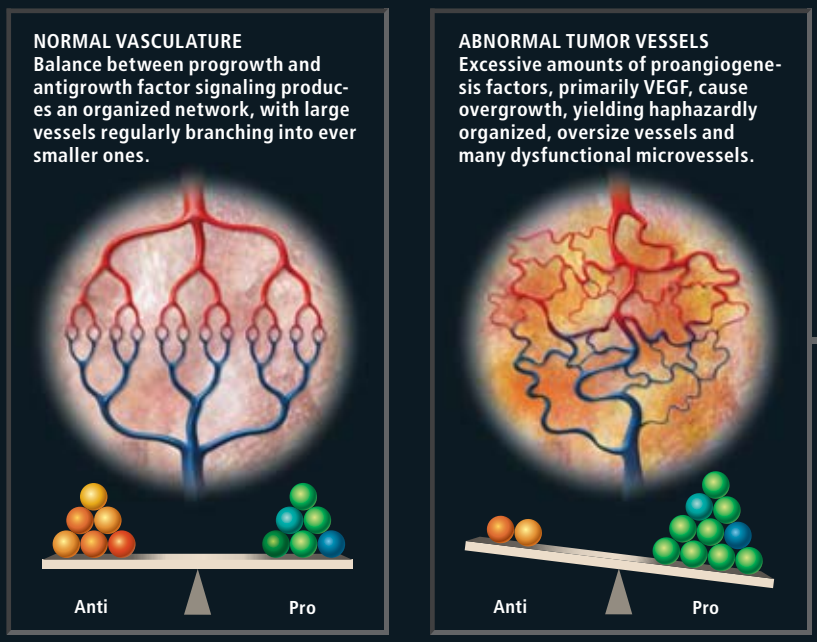
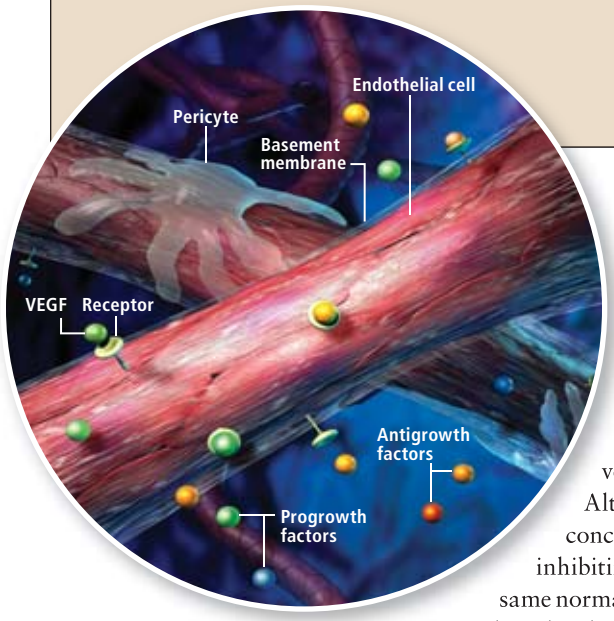
[A SOLUTION]

TIPPING THE BALANCE TOWARD NORMALCY

Restoring tumor vasculature to a more normal state optimizes conditions for anticancer therapies to reach tumor cells and to work more effectively. Many abnormalities arise in tumor vessels because factors that stimulate vessel growth, or angiogenesis, overwhelm growth inhibitors that usually check vessel proliferation. Antiangiogenesis drugs that suppress the primary progrowth factor, VEGF, tip the balance back toward normal vessel formation and maintenance. Normalization does not last indefinitely, because the drugs may ultimately destroy most vessels or a tumor may become resistant to them.



▼ **HEALTHY VESSEL GROWTH AND MAINTENANCE**
Endothelial cells form blood vessels in response to signals from molecules that promote and inhibit growth. Pericyte cells straddle vessels, and a basement membrane surrounds them; both provide support.



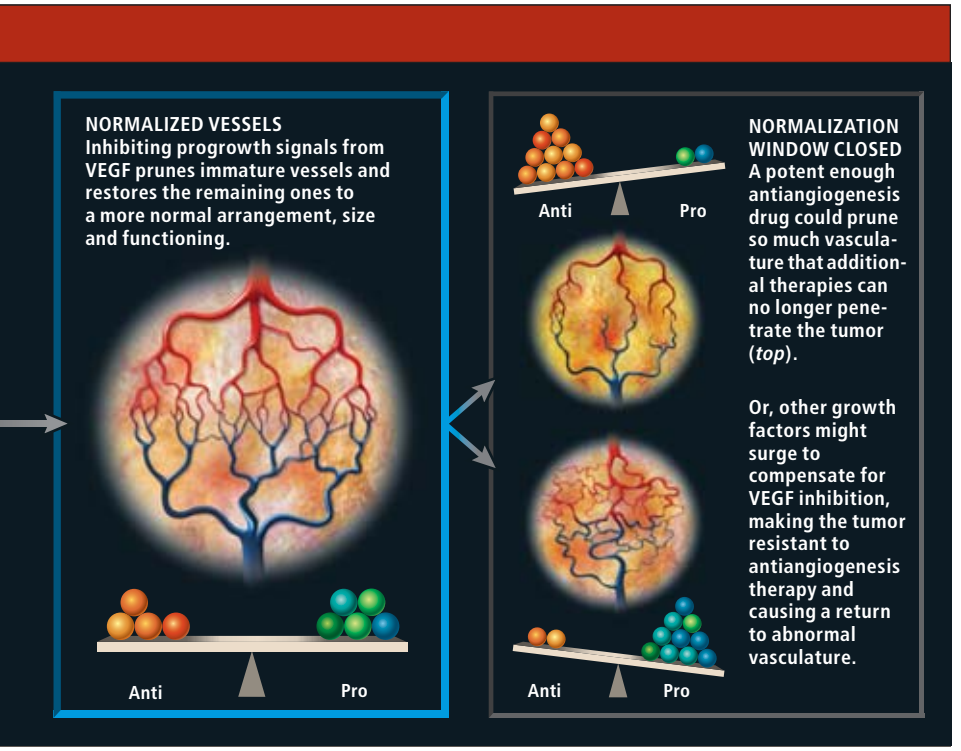
Normalized vessels make cells more vulnerable to the treatments that they can now deliver more efficiently.

Because VEGF is abundant in most solid tumors, I suspected that finding a way to mop up the excess VEGF or interfere with the growth signals it generates could restore balance and cause tumor vasculature to revert to a more normal state. Alternatively, increasing the concentration of angiogenesis-inhibiting factors could have the same normalizing effect on the blood vessels. I also theorized that vessels treated in either way would not remain normal forever—they would be destroyed if the inhibitors were potent enough or would become abnormal again if the tumors developed the ability to make different stimulators, such as basic fibroblast growth factor (bFGF), which can mimic many of the effects of VEGF. The only way to find out was to try angiogenesis inhibitors on tumors and see what happened.

In 1995 antibody-based drugs that could neutralize the effects of VEGF were already in development, so we were able to use these to test our approach in mice. Certain of the antibodies attached directly to VEGF, hindering its ability to send a growth signal to endothelial cells by binding to receptors on the cell surface. Other antibodies bound to the VEGF receptors themselves, preventing the growth factor from making contact. Remarkably, both forms of VEGF inhibition caused some of the immature and inefficient blood vessels characteristic of many tumors to be pruned away and induced the remaining vessels to remodel themselves so that they began to resemble normal vasculature. Those normalized blood vessels were less leaky, less dilated and less tortuous. We could also detect functional improvements in the tumors, including lower interstitial fluid pressure, higher oxygenation and improved penetration of drugs.

As excited as we were by these results and by the fact that they were later reproduced in animals by other researchers, we still could not know whether the same responses would occur in cancer patients. And many researchers were understandably skeptical of our approach. By the late 1990s, when I first proposed the idea of tumor vessel normalization publicly, scientists in academia and industry had been working on making drugs to destroy blood vessels. Their pursuit was based on the hypothesis put forward in 1971 by my Harvard colleague Judah Folkman that tumor growth could be halted by starving the mass using antiangiogenic drugs [see "Vessels of Death or Life," by Rakesh K. Jain and Peter Carmeliet; SCIENTIFIC AMERICAN, December 2001]. Indeed, the drug Avastin, approved by the U.S. Food and Drug Administra-

KEITH KASNOT (*illustrations*); JEN CHRISTIANSEN (*seesaws*); ADAPTED FROM ORIGINAL ILLUSTRATIONS BY LANCE L. MUNN IN "NORMALIZING TUMOR VASCULATURE WITH ANTI-ANGIOGENIC THERAPY: A NEW PARADIGM FOR COMBINATION THERAPY," BY RAKESH K. JAIN, IN *NATURE MEDICINE*, VOL. 7, NO. 9, SEPTEMBER 2001



tion for use in cancer treatment in 2004, is a VEGF-neutralizing antibody originally developed as such an antiangiogenesis agent.

In laboratory testing and clinical trials, Avastin has been shown to destroy blood vessels in animal and human tumors, although when used alone it does not increase overall survival in cancer patients. In a pivotal clinical trial that led to its approval, however, Avastin did increase the survival of patients with advanced colorectal cancer but *only* when it was used in conjunction with standard chemotherapy. That positive outcome seemed quite paradoxical at the time because, in principle, a drug that was designed and deployed to destroy blood vessels should reduce the effectiveness of chemotherapy, which requires functioning blood vessels to reach tumor cells. Some published studies have in fact shown that antiangiogenic agents can hinder radiation and chemotherapy. So how could these apparently contradictory findings be reconciled?

Our group had the chance to find out by closely examining the structure and function of blood vessels in the tumors of rectal cancer patients receiving Avastin and combined chemotherapy and radiation in a 2002 clinical trial supported by the National Cancer Institute and led by Christopher Willett, now at Duke University Medical Center. Very quickly, we saw that the changes to tumor vasculature in those patients were not limited to simple vessel destruction.

Two weeks after a single injection of Avastin, blood flow within the tumors did drop by 30 to 50 percent in six consecutive patients. The density of microvessels, the overall number of blood vessels and the interstitial fluid pressure in the tumors were all reduced as well. And a form of programmed cell death known as apoptosis, characteristic of oxygen and nutrient deprivation, increased among tumor cells that no longer had access to the pruned vasculature.

Surprisingly, however, there was no concurrent decrease in a sign of overall energy use by the tumor, its uptake of a glucose analogue, as might be expected if the tumor were only being starved. Instead it seemed that the remaining tumor vessels had become more efficient in supporting the energy needs of the surviving cancer cells. Furthermore, the rate of proliferation of cancer cells increased in some tumors, reflecting their access to better-functioning vessels and a more normal tissue microenvironment. Although increased proliferation is usually not desirable when it comes to cancer cells, that state would make them more sensitive to chemotherapy drugs, which generally target dividing cells.

Together these results provided a first glimpse of how a drug like Avastin works in patients and thereby revealed why it might improve the outcome of radiation or chemotherapy for a time. As the drug blocks the effects of VEGF, some tumor vasculature is pruned away immediately, but the vessels that remain become less abnormal. In addition to improving the overall tumor microenvironment, those normalized vessels also make the surviving cells more vulnerable to the treatments that they can now deliver more efficiently. Restoring normal function to tumor vessels thereby creates a period during which treatment with a variety of cancer therapies should be maximally effective.

TUMOR VESSELS cast in polymer from a surgically excised colon cancer form a dense crystalline mass representing a chaotic profusion of microvessels. In contrast, large gaps indicate areas of the tumor that lacked any blood supply.

FROM "GEOMETRIC RESISTANCE AND MICROVASCULAR NETWORK ARCHITECTURE OF HUMAN COLORECTAL CARCINOMA," BY J. R. LESS, M. C. POSNER, T. C. SKALAK, N. WOLMARK AND R. K. JAIN, IN *MICROCIRCULATION*, VOL. 4, NO. 1; 1997

Window of Opportunity

To truly benefit from this new insight into the way that antiangiogenic therapy can work with radiation or chemotherapies, an oncologist would need to know when a patient's tumor vessels first begin to normalize and how long they remain that way. My research group returned to experimenting with mice to better characterize this period we came to call the "normalization window." We treated brain tumors in the animals with an antibody designed to block the main VEGF receptor used by endothelial cells and saw signs of vessel normalization begin after one day. During the normalization window—which lasted only about five to six days—tumor oxygenation increased and radiation therapy yielded the best therapeutic outcome. Other teams working with laboratory animals have subsequently reported similar observations.

Enough evidence supported this model, in fact, that we were able to test it in another National Cancer Institute clinical trial, completed just over a year ago. Led by my Massachusetts General Hospital colleagues Tracy Batchelor and Gregory Sorensen, the trial included 30 patients whose brain tumors, known as glioblastomas, had regrown despite aggressive surgery, radiation and chemotherapy. These patients had a life expectancy of less than six months.

They received a daily oral dose of Recentin, an experimental drug that potently inhibits the three primary cellular receptors for VEGF. Using advanced imaging techniques, we were able to look for effects in their tumors and saw them almost immediately [*see illustration on opposite page*]. The signs of vascular normalization included reduced vessel diameter and leakiness, which continued for at least 28 days, with some normalized characteristics persisting for the entire four-month duration of the study. Moreover, as anticipated by our original model, the normalization was accompanied by a rapid decrease in swelling in and around the tumor, an effect that continued as long as the patients took the Recentin. Because the side effects of VEGF inhibition can be severe, however, some patients asked for a break from the treatment during the trial, which allowed us to observe the tumor vessels becoming abnormal again when Recentin was discontinued, and renormalized when the drug was resumed.

These results were the first to define how long the period of vascular normalization can last in humans and have led to a much larger ongoing clinical trial involving 300 patients to further define the role that Recentin, with and without chemotherapy, might play in the treatment of glioblastoma. We are also studying a number of antiangiogenic drugs in combination with traditional therapies in newly diagnosed and recurrent tumor cases in more types of cancer.

At the same time, we are also investigating ways of expanding the window of normalization so that survival improvements can be extended from months to years. Any potential strategy to repair vessels must recognize that VEGF blockade alone may not always be sufficient to achieve or sustain normalization, because tumors can substitute other growth factors to get around the loss of VEGF signaling. As tumors grow larger, for instance, they tend to make a diverse array of proangiogenic molecules in addition to VEGF, so their vessels may gradually lose responsiveness to a treatment such as Avastin.

In rectal cancer patients, for instance, our

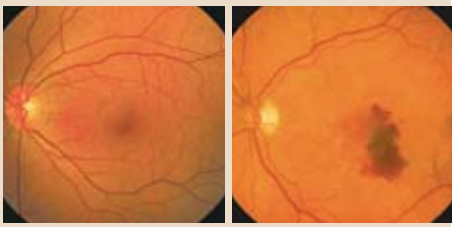
Vessel Repair: Beyond Cancer

Hundreds of millions of people around the world suffer from noncancerous conditions that involve abnormal vasculature. Modifying blood vessel growth and function might become a key component of the therapeutic arsenal for those diseases as well, so drugs that normalize blood vessels have the potential to vastly impact human health.

Among the most widespread of problems in this category, for example, is atherosclerosis, an artery disease whose features include an accumulation of fatty plaques within the inner walls of blood vessels. Inside such plaques, inflammation-inducing blood cells and other detritus accumulate, gradually enlarging the lesion. New blood vessels sprout within this growing mass to feed it, much like a tumor. These new vessels also share many abnormal features with tumor vessels, such as leakiness and disorganization. In principle, therefore, applying antiangiogenic agents should normalize intraplaque vessels, stabilizing the lesions, halting their expansion and reducing their potential for rupture.

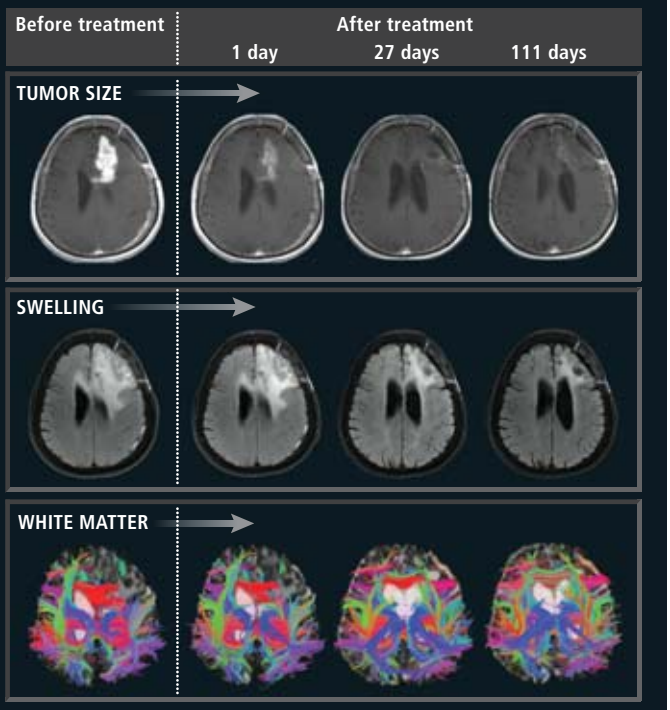
Eye diseases such as diabetic retinopathy and the so-called wet form of age-related macular degeneration (AMD) are also characterized by vascular abnormalities similar to those seen in tumors. A hallmark of wet AMD is, in fact, the leakiness of blood vessels in the retina at the back of the eye. As a result, blood oozes into surrounding tissue, causing partial or total vision loss. More than nine million Americans are currently affected. Not surprisingly, the greatest progress outside the realm of cancer treatment in using antiangiogenesis to repair vascular abnormalities has been in wet AMD. Two drugs, Lucentis and Macugen—both inhibitors of VEGF—have already been approved for treating the condition and most likely work by normalizing the leaky vessels.

These same normalization principles may also be useful for controlling conditions that cause fluid buildup (edema) and for tissue engineering and regenerative medicine, which require the creation and maintenance of normally functioning vasculature. —***R.K.J.***



WET AMD affects the macula, a region of the retina at the back of the eye that appears slightly darkened in a healthy human eye (*left*) but can sprout excess blood vessels leading to macular degeneration. The abnormal vessels leak blood (*right*) into surrounding tissue, obscuring vision.

KANG ZHANG AND JAMES GILMAN



BRAIN TUMOR response to antiangiogenesis therapy reflects some effects of vascular normalization. MRI images of a patient's brain one day before beginning treatment and at subsequent intervals show a shrinking white area corresponding to the malignant tumor's location (*top row*). Another set of views highlights accumulated fluid in the same area receding (*middle row*). As tumor-generated edema diminishes, reduced compression of brain tissue is visible in the rebounding of fibrous white matter tracts, which are color-coded here by brain region (*bottom row*).

The ability to use these drugs for vascular repair makes them valuable tools for attacking tumors in more than one way.

group discovered that blood levels of VEGF and PlGF (placental growth factor), a related molecule, actually increased after VEGF was mopped up with Avastin, suggesting that the tumor or other tissues began manufacturing more of those factors in response. And in recurrent glioblastoma patients, blood levels of multiple proangiogenic molecules rose as tumors escaped the Recentin treatment.

This diversification of progrowth signals illustrates that the challenge for the oncologist will be to formulate cocktails of agents specifically tailored to the molecular profile of each patient's primary and metastatic tumors and to changes in those profiles that will likely occur over time. It is worth noting, however, that the available tools for promoting vascular normalization are not limited to drugs targeting VEGF or other growth factors directly. We have shown in mice, for example, that the drug Herceptin—an antibody that targets a tumor cell-surface protein called HER2 and that is given to about a quarter of women with breast cancer—can mimic the responses produced by an antiangiogenic cocktail and normalize tumor vessels. Herceptin indirectly lowers cellular manufacture of several proangiogenic molecules while increasing the cells' production of the antiangiogenic thrombospondin-1.

In addition to identifying new and existing medications that can foster vascular normalization, it will be important to find minimally invasive and affordable ways for doctors to monitor the normalization process, to best exploit it when delivering treatments. To that end, my colleagues and I have been working to identify so-called biomarkers: readily identifiable signs that reflect what is happening inside the tumor and thereby reveal the onset and duration of the normalization window in individual patients. Such markers might include, for example, proteins in the bloodstream or in urine whose levels rise or fall during this time window.

Finding that antiangiogenesis drugs can normalize vasculature should not suggest that the original purpose for which they were developed is no longer valid. If a drug is sufficiently potent and specific to destroy enough tumor vasculature to starve the entire tumor and save a patient's life, then that would be a happy outcome for everyone. But the ability to use these drugs for vascular repair as well makes them valuable tools for attacking tumors in more than one way. In the longer term, this research can also benefit the many millions of people around the world suffering from other diseases caused by abnormal vasculature, such as age-related macular degeneration and atherosclerosis [*see box on opposite page*].

More than 30 years ago, when I first set out to understand the tortuous and dysfunctional blood vessels of tumors, I never imagined where that road would lead. Nor could I have pictured a day when a patient with a disease of abnormal blood vessels could walk into a clinic, have various biomarkers measured, then receive a tailored regimen of normalizing drugs to repair those vessels. But now that day looks closer than ever before. ■

MORE TO EXPLORE

Normalization of the Tumor Vasculature: An Emerging Concept in Anti-Angiogenic Therapy. Rakesh K. Jain in *Science,* Vol. 307, pages 58–62; January 2005.

Lessons from Phase III Clinical Trials of Anti-VEGF Therapy for Cancer. Rakesh K. Jain, Dan G. Duda, Jeffrey W. Clark and Jay S. Loeffler in *Nature Clinical Practice Oncology,* Vol. 3, No. 1, pages 24–40; January 2006.

Angiogenesis in Brain Tumors. Rakesh K. Jain et al. in *Nature Reviews Neuroscience,* Vol. 8, pages 610–622; August 2007.

Antiangiogenic Therapy for Normalization of Atherosclerotic Plaque Vasculature: A Potential Strategy for Plaque Stabilization. Rakesh K. Jain et al. in *Nature Clinical Practice Cardiovascular Medicine,* Vol. 4, No. 9, pages 491–503; September 2007.

For more articles by Rakesh K. Jain and animations explaining vessel normalization, go to **http://steele.mgh.harvard.edu/**

FROM "AZD2171, A PAN-VEGF RECEPTOR TYROSINE KINASE INHIBITOR, NORMALIZES TUMOR VASCULATURE AND ALLEVIATES EDEMA IN GLIOBLASTOMA PATIENTS," BY T. BATCHELOR ET AL., IN *CANCER CELL*, VOL. 11, JANUARY 2007. © 2007 REPRINTED WITH PERMISSION OF ELSEVIER

By 2050 solar power could end U.S. dependence on foreign oil and slash greenhouse gas emissions

By Ken Zweibel, James Mason and Vasilis Fthenakis

KEY CONCEPTS

- A massive switch from coal, oil, natural gas and nuclear power plants to solar power plants could supply 69 percent of the U.S.'s electricity and 35 percent of its total energy by 2050.
- A vast area of photovoltaic cells would have to be erected in the Southwest. Excess daytime energy would be stored as compressed air in underground caverns to be tapped during nighttime hours.
- Large solar concentrator power plants would be built as well.
- A new direct-current power transmission backbone would deliver solar electricity across the country.
- But $420 billion in subsidies from 2011 to 2050 would be required to fund the infrastructure and make it cost-competitive.

—The Editors

High prices for gasoline and home heating oil are here to stay. The U.S. is at war in the Middle East at least in part to protect its foreign oil interests. And as China, India and other nations rapidly increase their demand for fossil fuels, future fighting over energy looms large. In the meantime, power plants that burn coal, oil and natural gas, as well as vehicles everywhere, continue to pour millions of tons of pollutants and greenhouse gases into the atmosphere annually, threatening the planet.

Well-meaning scientists, engineers, economists and politicians have proposed various steps that could slightly reduce fossil-fuel use and emissions. These steps are not enough. The U.S. needs a bold plan to free itself from fossil fuels. Our analysis convinces us that a massive switch to solar power is the logical answer.

Solar energy's potential is off the chart. The energy in sunlight striking the earth for 40 minutes is equivalent to global energy consumption for a year. The U.S. is lucky to be endowed with a vast resource; at least 250,000 square miles of land in the Southwest alone are suitable for constructing solar power plants, and that land receives more than 4,500 quadrillion British thermal units (Btu) of solar radiation a year. Converting only 2.5 percent of that radiation into electricity would match the nation's total energy consumption in 2006.

To convert the country to solar power, huge tracts of land would have to be covered with photovoltaic panels and solar heating troughs. A direct-current (DC) transmission backbone would also have to be erected to send that energy efficiently across the nation.

The technology is ready. On the following pages we present a grand plan that could provide 69 percent of the U.S.'s electricity and 35 percent of its total energy (which includes transportation) with solar power by 2050. We project that this energy could be sold to consumers at rates equivalent to today's rates for conventional power sources, about five cents per kilowatt-hour (kWh). If wind, biomass and geothermal sources were also developed, renewable energy could provide 100 percent of the nation's electricity and 90 percent of its energy by 2100.

The federal government would have to invest more than $400 billion over the next 40 years to complete the 2050 plan. That investment is substantial, but the payoff is greater. Solar plants consume little or no fuel, saving billions of dollars year after year. The infrastructure would displace 300 large coal-fired power plants and 300 more large natural gas plants and all the fuels they consume. The plan would effectively eliminate all imported oil, fundamentally cutting U.S. trade deficits and easing political tension in the Middle East

SCHOTT AG/COMMERCIAL HANDOUT/EPA/CORBIS

A

Solar Grand Plan

and elsewhere. Because solar technologies are almost pollution-free, the plan would also reduce greenhouse gas emissions from power plants by 1.7 billion tons a year, and another 1.9 billion tons from gasoline vehicles would be displaced by plug-in hybrids refueled by the solar power grid. In 2050 U.S. carbon dioxide emissions would be 62 percent below 2005 levels, putting a major brake on global warming.

Photovoltaic Farms

In the past few years the cost to produce photovoltaic cells and modules has dropped significantly, opening the way for large-scale deployment. Various cell types exist, but the least expensive modules today are thin films made of cadmium telluride. To provide electricity at six cents per kWh by 2020, cadmium telluride modules would have to convert electricity with 14 percent efficiency, and systems would have to be installed at $1.20 per watt of capacity. Current modules have 10 percent efficiency and an installed system cost of about $4 per watt. Progress is clearly needed, but the technology is advancing quickly; commercial efficiencies have risen from 9 to 10 percent in the past 12 months. It is worth noting, too, that as modules improve, rooftop photovoltaics will become more cost-competitive for homeowners, reducing daytime electricity demand.

In our plan, by 2050 photovoltaic technology would provide almost 3,000 gigawatts (GW), or billions of watts, of power. Some 30,000 square miles of photovoltaic arrays would have to be erected. Although this area may sound enormous, installations already in place indicate that the land required for each gigawatt-hour of solar energy produced in the Southwest is less than that needed for a coal-powered plant when factoring in land for coal mining. Studies by the National Renewable Energy Laboratory in Golden, Colo., show that more than enough land in the Southwest is available without requiring use of environmentally sensitive areas, population centers or difficult terrain. Jack Lavelle, a spokesperson for Arizona's Department of Water Conservation, has noted that more than 80 percent of his state's land is not privately owned and that Arizona is very interested in developing its solar potential. The benign nature of photovoltaic plants (including no water consumption) should keep environmental concerns to a minimum.

The main progress required, then, is to raise module efficiency to 14 percent. Although the

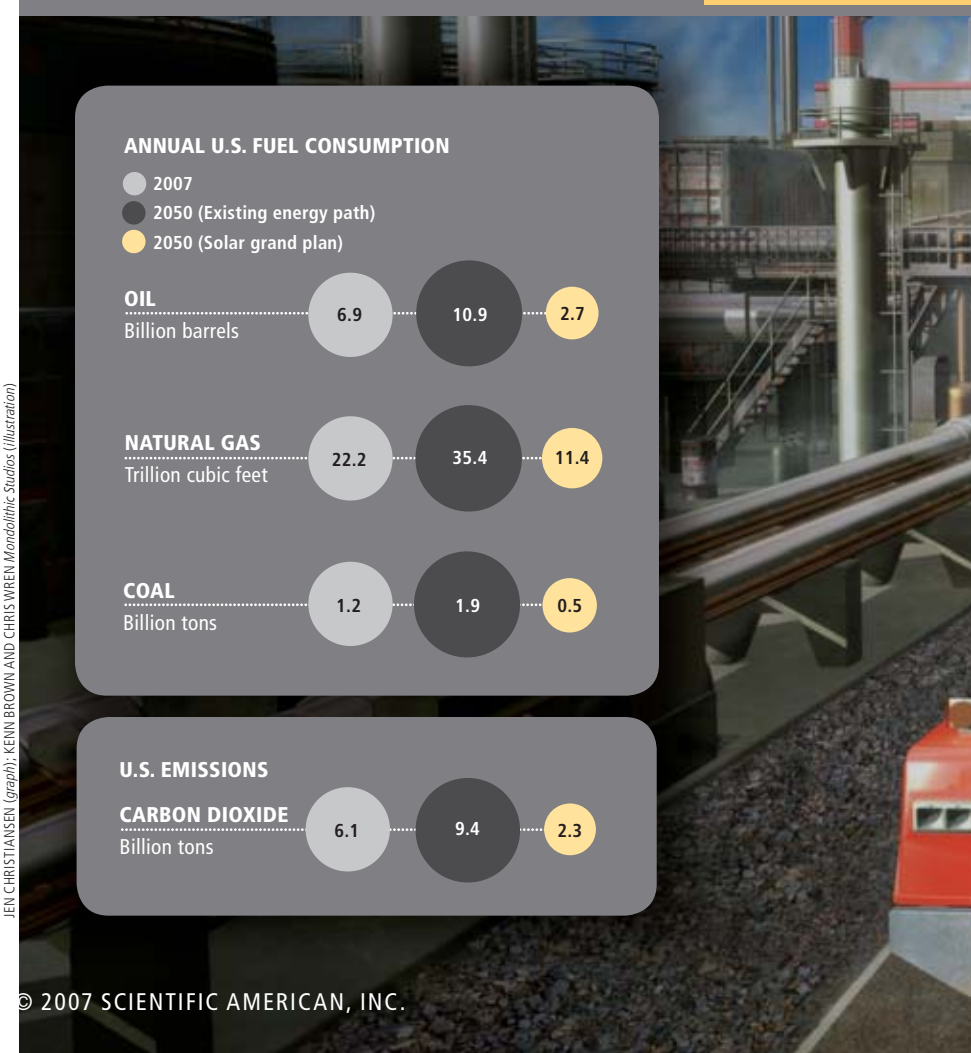
U.S. Plan for 2050

Solar Power Provides . . .

69% of electricity | **35%** of total energy

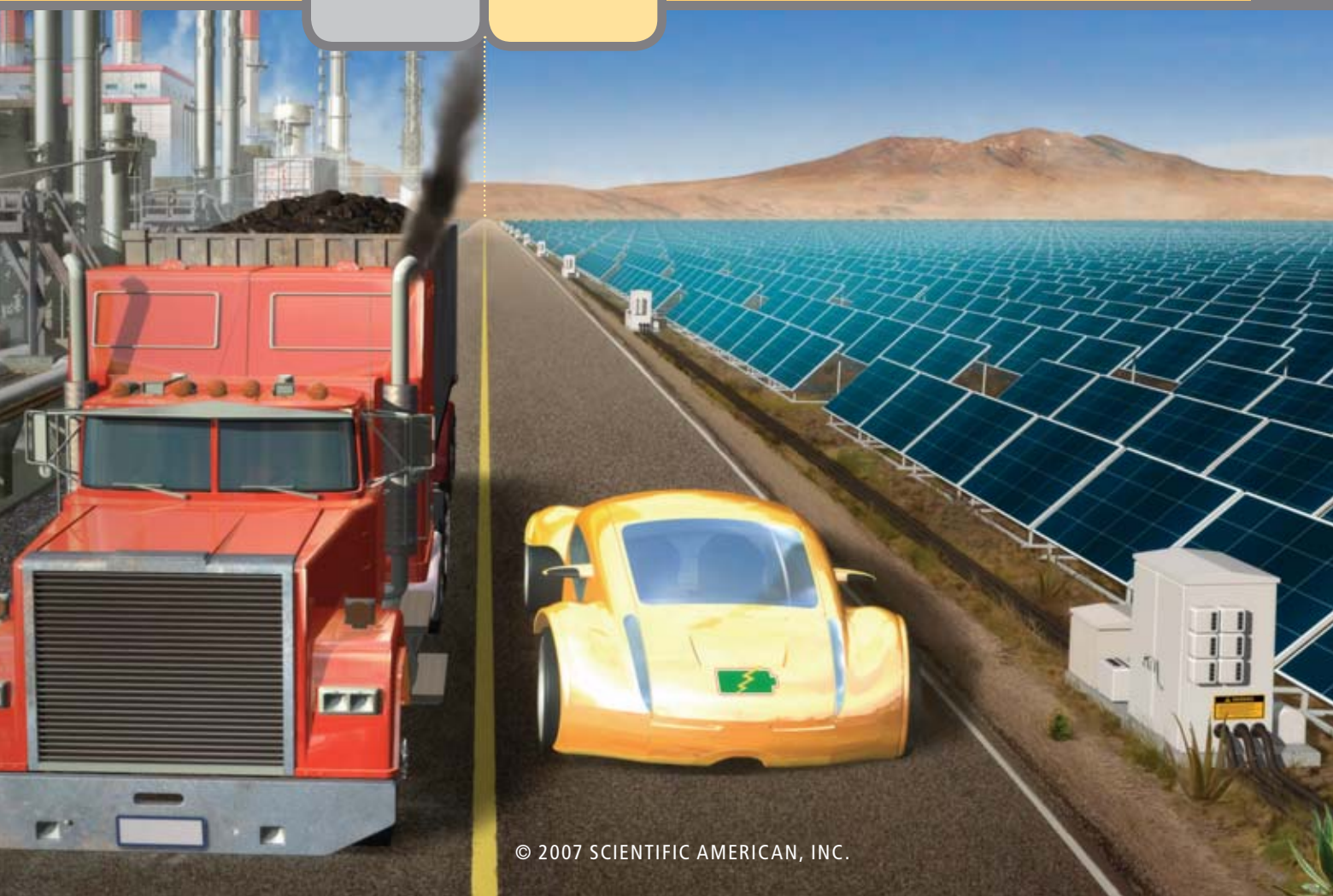
By 2050 vast photovoltaic arrays in the Southwest would supply electricity instead of fossil-fueled power plants and would also power a widespread conversion to plug-in electric vehicles. Excess energy would be stored as compressed air in underground caverns. Large arrays that concentrate sunlight to heat water would also supply electricity. A new high-voltage, direct-current transmission backbone would carry power to regional markets nationwide. The technologies and factors critical to their success are summarized at the right, along with the extent to which the technologies must be deployed by 2050. The plan would substantially cut the country's consumption of fossil fuels and its emission of greenhouse gases (*below*). We have assumed a 1 percent annual growth in net energy demand. And we have anticipated improvements in solar technologies forecasted only until 2020, with no further gains beyond that date. *—K.Z., J.M. and V.F.*

TECHNOLOGY
PHOTOVOLTAICS
COMPRESSED-AIR ENERGY STORAGE (with photovoltaic electricity)
CONCENTRATED SOLAR POWER
DC TRANSMISSION



JEN CHRISTIANSEN (*graph*); KENN BROWN AND CHRIS WREN *Mondolithic Studios* (*illustration*)

CRITICAL FACTOR	2007	2050	ADVANCES NEEDED
Land area	10 sq miles	30,000 sq miles	Policies to develop large public land areas
Thin-film module efficiency	10%	14%	More transparent materials to improve light transmission; more densely doped layers to increase voltage; larger modules to reduce inactive area
Installed cost	$4/W	$1.20/W	Improvements in module efficiency; gains from volume production
Electricity price	16¢/kWh	5¢/kWh	Follows from lower installed cost
Total capacity	0.5 GW	2,940 GW	National energy plan built around solar power
Volume	0	535 billion cu ft	Coordination of site development with natural gas industry
Installed cost	$5.80/W	$3.90/W	Economies of scale; decreasing photovoltaic electricity prices
Electricity price	20¢/kWh	9¢/kWh	Follows from lower installed cost
Total capacity	0.1 GW	558 GW	National energy plan
Land area	10 sq miles	16,000 sq miles	Policies to develop large public land areas
Solar-to-electric efficiency	13%	17%	Fluids that transfer heat more effectively
Installed cost	$5.30/W	$3.70/W	Single-tank thermal storage systems; economies of scale
Electricity price	18¢/kWh	9¢/kWh	Follows from lower installed cost
Total capacity	0.5 GW	558 GW	National energy plan
Length	500 miles	100,000–500,000 miles	New high-voltage DC grid from Southwest to rest of country



By 2100 renewable energy could generate 100 percent of the U.S.'s electricity and more than 90 percent of its energy.

efficiencies of commercial modules will never reach those of solar cells in the laboratory, cadmium telluride cells at the National Renewable Energy Laboratory are now up to 16.5 percent and rising. At least one manufacturer, First Solar in Perrysburg, Ohio, increased module efficiency from 6 to 10 percent from 2005 to 2007 and is reaching for 11.5 percent by 2010.

Pressurized Caverns

The great limiting factor of solar power, of course, is that it generates little electricity when skies are cloudy and none at night. Excess power must therefore be produced during sunny hours and stored for use during dark hours. Most energy storage systems such as batteries are expensive or inefficient.

Compressed-air energy storage has emerged as a successful alternative. Electricity from photovoltaic plants compresses air and pumps it into vacant underground caverns, abandoned mines, aquifers and depleted natural gas wells. The pressurized air is released on demand to turn a turbine that generates electricity, aided by burning small amounts of natural gas. Compressed-air energy storage plants have been operating reliably in Huntorf, Germany, since 1978 and in McIntosh, Ala., since 1991. The turbines burn only 40 percent of the natural gas they would if they were fueled by natural gas alone, and better heat recovery technology would lower that figure to 30 percent.

Studies by the Electric Power Research Institute in Palo Alto, Calif., indicate that the cost of compressed-air energy storage today is about half that of lead-acid batteries. The research indicates that these facilities would add three or four cents per kWh to photovoltaic generation, bringing the total 2020 cost to eight or nine cents per kWh.

Electricity from photovoltaic farms in the Southwest would be sent over high-voltage DC transmission lines to compressed-air storage facilities throughout the country, where turbines would generate electricity year-round. The key is to find adequate sites. Mapping by the natural gas industry and the Electric Power Research Institute shows that suitable geologic formations exist in 75 percent of the country, often close to metropolitan areas. Indeed, a compressed-air energy storage system would look similar to the U.S. natural gas storage system. The industry stores eight trillion cubic feet of gas in 400 underground reservoirs. By 2050 our plan would require 535 billion cubic feet of storage, with air pressurized at 1,100 pounds per square inch. Although development will be a challenge, plenty of reservoirs are available,

TUCSON ELECTRIC POWER COMPANY

Photovoltaics

In the 2050 plan vast photovoltaic farms would cover 30,000 square miles of otherwise barren land in the Southwest. They would resemble Tucson Electric Power Company's 4.6-megawatt plant in Springerville, Ariz., which began in 2000 (*left*). In such farms, many photovoltaic cells are interconnected on one module, and modules are wired together to form an array (*right*). The direct current from each array flows to a transformer that sends it along high-voltage lines to the power grid. In a thin-film cell (*inset*), the energy of incoming photons knocks loose electrons in the cadmium telluride layer; they cross a junction, flow to the top conductive layer and then flow around to the back conductive layer, creating current.

and it would be reasonable for the natural gas industry to invest in such a network.

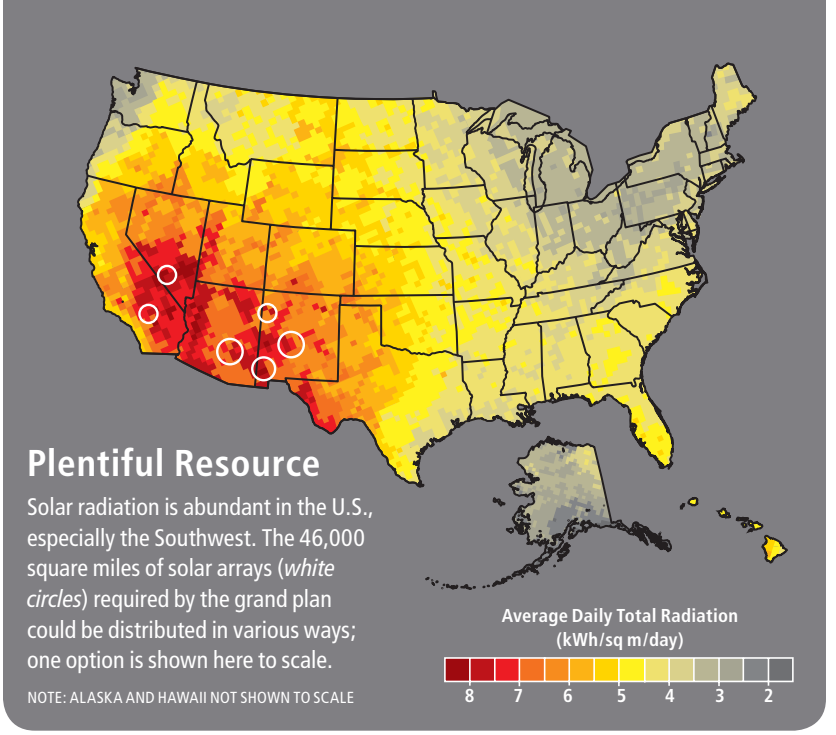
Hot Salt

Another technology that would supply perhaps one fifth of the solar energy in our vision is known as concentrated solar power. In this design, long, metallic mirrors focus sunlight onto a pipe filled with fluid, heating the fluid like a huge magnifying glass might. The hot fluid runs through a heat exchanger, producing steam that turns a turbine.

For energy storage, the pipes run into a large, insulated tank filled with molten salt, which retains heat efficiently. Heat is extracted at night, creating steam. The molten salt does slowly cool, however, so the energy stored must be tapped within a day.

Nine concentrated solar power plants with a total capacity of 354 megawatts (MW) have been generating electricity reliably for years in the U.S. A new 64-MW plant in Nevada came online in March 2007. These plants, however, do not have heat storage. The first commercial installation to incorporate it—a 50-MW plant with seven hours of molten salt storage—is being constructed in Spain, and others are being designed around the world. For our plan, 16 hours of storage would be needed so that electricity could be generated 24 hours a day.

Existing plants prove that concentrated solar power is practical, but costs must decrease. Economies of scale and continued research would help. In 2006 a report by the Solar Task Force of the Western Governors' Association concluded that concentrated solar power could provide electricity at 10 cents per kWh or less by 2015 if 4 GW of plants were constructed. Finding ways to boost the temperature of heat exchanger fluids would raise operating efficiency,



Plentiful Resource

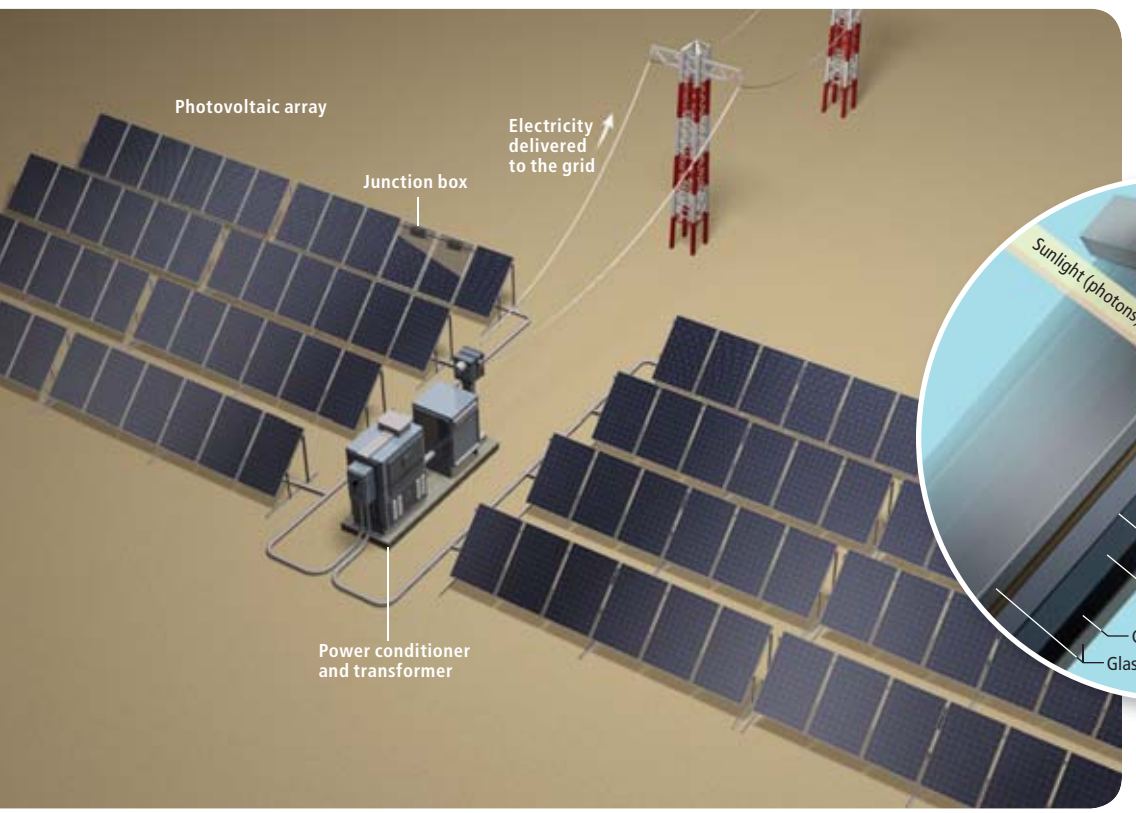
Solar radiation is abundant in the U.S., especially the Southwest. The 46,000 square miles of solar arrays (*white circles*) required by the grand plan could be distributed in various ways; one option is shown here to scale.

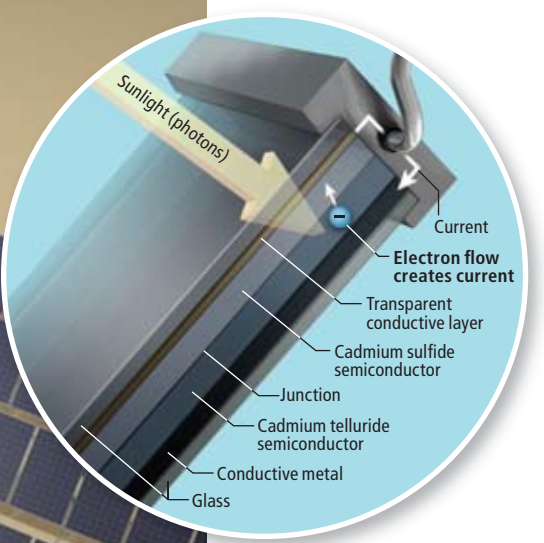
NOTE: ALASKA AND HAWAII NOT SHOWN TO SCALE

SOURCE FOR MAP: COURTESY OF NATIONAL RENEWABLE ENERGY LABORATORY; DON FOLEY (*illustrations*)

PAYOFFS

- Foreign oil dependence cut from 60 to 0 percent
- Global tensions eased and military costs lowered
- Massive trade deficit reduced significantly
- Greenhouse gas emissions slashed
- Domestic jobs increased





too. Engineers are also investigating how to use molten salt itself as the heat-transfer fluid, reducing heat losses as well as capital costs. Salt is corrosive, however, so more resilient piping systems are needed.

Concentrated solar power and photovoltaics represent two different technology paths. Neither is fully developed, so our plan brings them both to large-scale deployment by 2020, giving them time to mature. Various combinations of solar technologies might also evolve to meet demand economically. As installations expand, engineers and accountants can evaluate the pros and cons, and investors may decide to support one technology more than another.

Direct Current, Too

The geography of solar power is obviously different from the nation's current supply scheme. Today coal, oil, natural gas and nuclear power plants dot the landscape, built relatively close to where power is needed. Most of the country's solar generation would stand in the Southwest. The existing system of alternating-current (AC) power lines is not robust enough to carry power from these centers to consumers everywhere and would lose too much energy over long hauls. A new high-voltage, direct-current (HVDC) power transmission backbone would have to be built.

Studies by Oak Ridge National Laboratory indicate that long-distance HVDC lines lose far less energy than AC lines do over equivalent spans. The backbone would radiate from the Southwest toward the nation's borders. The lines would terminate at converter stations where the power would be switched to AC and sent along existing regional transmission lines that supply customers.

The AC system is also simply out of capacity, leading to noted shortages in California and other regions; DC lines are cheaper to build and require less land area than equivalent AC lines. About 500 miles of HVDC lines operate in the U.S. today and have proved reliable and efficient. No major technical advances seem to be needed, but more experience would help refine operations. The Southwest Power Pool of Texas is designing an integrated system of DC and AC transmission to enable development of 10 GW of wind power in western Texas. And TransCanada, Inc., is proposing 2,200 miles of HVDC lines to carry wind energy from Montana and Wyoming south to Las Vegas and beyond.

PINCH POINTS

- **Subsidies totaling $420 billion through 2050**
- **Political leadership needed to raise the subsidy, possibly with a carbon tax**
- **New high-voltage, direct-current electric transmission system built profitably by private carriers**

Stage One: Present to 2020

We have given considerable thought to how the solar grand plan can be deployed. We foresee two distinct stages. The first, from now until 2020, must make solar competitive at the mass-production level. This stage will require the government to guarantee 30-year loans, agree to purchase power and provide price-support subsidies. The annual aid package would rise steadily from 2011 to 2020. At that time, the solar technologies would compete on their own merits. The cumulative subsidy would total $420 billion (we will explain later how to pay this bill).

About 84 GW of photovoltaics and concentrated solar power plants would be built by 2020. In parallel, the DC transmission system would be laid. It would expand via existing rights-of-way along interstate highway corridors, minimizing land-acquisition and regulatory hurdles. This backbone would reach major markets in Phoenix, Las Vegas, Los Angeles and San Diego to the west and San Antonio, Dallas, Houston, New Orleans, Birmingham, Ala., Tampa, Fla., and Atlanta to the east.

Building 1.5 GW of photovoltaics and 1.5 GW of concentrated solar power annually in the first five years would stimulate many manufacturers to scale up. In the next five years, annual

POWERSOUTH ENERGY COOPERATIVE

construction would rise to 5 GW apiece, helping firms optimize production lines. As a result, solar electricity would fall toward six cents per kWh. This implementation schedule is realistic; more than 5 GW of nuclear power plants were built in the U.S. each year from 1972 to 1987. What is more, solar systems can be manufactured and installed at much faster rates than conventional power plants because of their straightforward design and relative lack of environmental and safety complications.

Stage Two: 2020 to 2050

It is paramount that major market incentives remain in effect through 2020, to set the stage for self-sustained growth thereafter. In extending our model to 2050, we have been conservative. We do not include any technological or cost improvements beyond 2020. We also assume that energy demand will grow nationally by 1 percent a year. In this scenario, by 2050 solar power plants will supply 69 percent of U.S. electricity and 35 percent of total U.S. energy. This quantity includes enough to supply all the electricity consumed by 344 million plug-in hybrid vehicles, which would displace their gasoline counterparts, key to reducing dependence on foreign oil and to mitigating greenhouse gas emissions. Some three million new domestic jobs—notably in manufacturing solar components—would be created, which is several times the number of U.S. jobs that would be lost in the then dwindling fossil-fuel industries.

The huge reduction in imported oil would lower trade balance payments by $300 billion a year, assuming a crude oil price of $60 a barrel (average prices were higher in 2007). Once solar power plants are installed, they must be maintained and repaired, but the price of sunlight is forever free, duplicating those fuel savings year after year. Moreover, the solar investment would enhance national energy security, reduce financial burdens on the military, and greatly decrease the societal costs of pollution and global warming, from human health problems to the ruining of coastlines and farmlands.

Ironically, the solar grand plan would lower energy consumption. Even with 1 percent annual growth in demand, the 100 quadrillion Btu consumed in 2006 would *fall* to 93 quadrillion Btu by 2050. This unusual offset arises because a good deal of energy is consumed to extract and process fossil fuels, and more is wasted in burning them and controlling their emissions.

To meet the 2050 projection, 46,000 square miles of land would be needed for photovoltaic and concentrated solar power installations. That area is large, and yet it covers just 19 percent of

[THE AUTHORS]

Ken Zweibel, James Mason and Vasilis Fthenakis met a decade ago while working on life-cycle studies of photovoltaics. Zweibel is president of PrimeStar Solar in Golden, Colo., and for 15 years was manager of the National Renewable Energy Laboratory's Thin-Film PV Partnership. Mason is director of the Solar Energy Campaign and the Hydrogen Research Institute in Farmingdale, N.Y. Fthenakis is head of the Photovoltaic Environmental Research Center at Brookhaven National Laboratory and is a professor in and director of Columbia University's Center for Life Cycle Analysis.

SCI AM

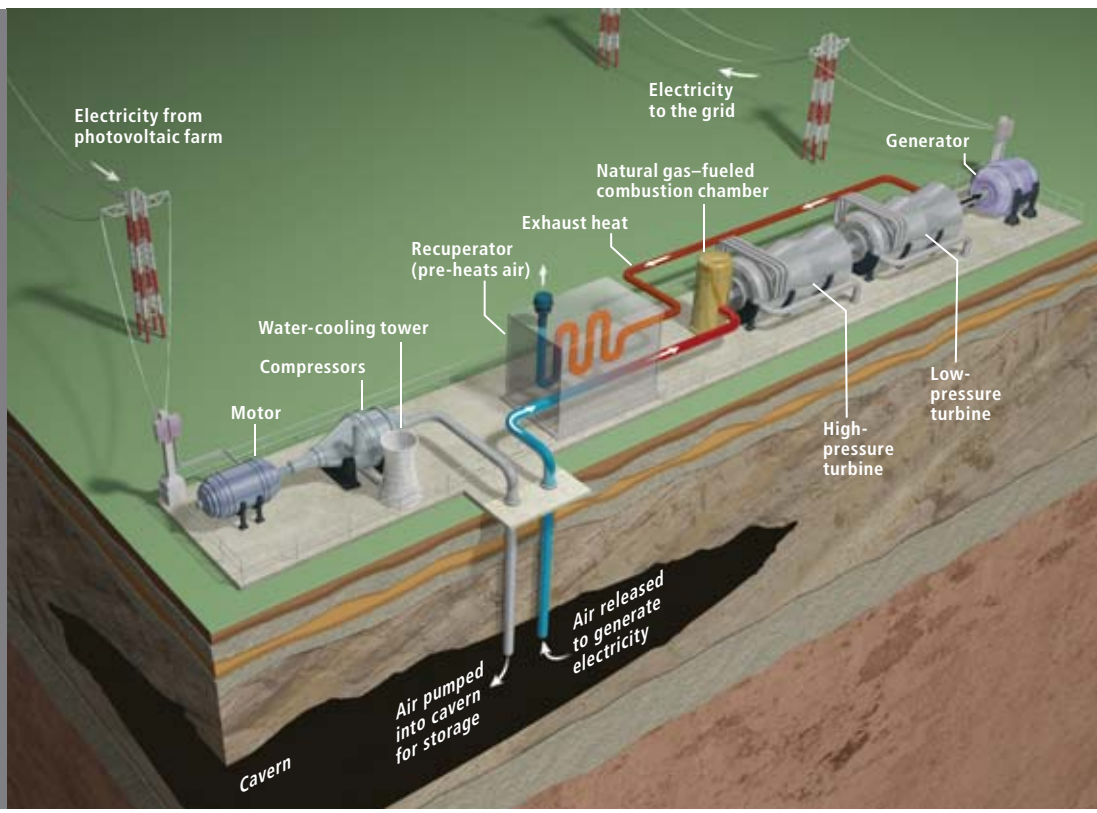
Brilliant? Far-fetched?

For a discussion with the authors about the solar grand plan, please visit our Community page at **http://science-community.SciAm.com**; click on Discussions, then Technology.

DON FOLEY

Underground Storage

Excess electricity produced during the day by photovoltaic farms would be sent over power lines to compressed-air energy storage sites close to cities. At night the sites would generate power for consumers. Such technology is already available; the PowerSouth Energy Cooperative's plant in McIntosh, Ala. (*left*), has operated since 1991 (the white pipe sends air underground). In these designs, incoming electricity runs motors and compressors that pressurize air and send it into vacant caverns, mines or aquifers (*right*). When the air is released, it is heated by burning small amounts of natural gas; the hot, expanding gases turn turbines that generate electricity.



Although $420 billion is substantial, it is less than the U.S. Farm Price Support program.

the suitable Southwest land. Most of that land is barren; there is no competing use value. And the land will not be polluted. We have assumed that only 10 percent of the solar capacity in 2050 will come from distributed photovoltaic installations—those on rooftops or commercial lots throughout the country. But as prices drop, these applications could play a bigger role.

2050 and Beyond

Although it is not possible to project with any exactitude 50 or more years into the future, as an exercise to demonstrate the full potential of solar energy we constructed a scenario for 2100. By that time, based on our plan, total energy demand (including transportation) is projected to be 140 quadrillion Btu, with seven times today's electric generating capacity.

To be conservative, again, we estimated how much solar plant capacity would be needed under the historical worst-case solar radiation conditions for the Southwest, which occurred during the winter of 1982–1983 and in 1992 and 1993 following the Mount Pinatubo eruption, according to National Solar Radiation Data Base records from 1961 to 2005. And again, we did not assume any further technological and cost improvements beyond 2020, even though it is nearly certain that in 80 years ongoing research would improve solar efficiency, cost and storage.

Under these assumptions, U.S. energy demand could be fulfilled with the following capacities: 2.9 terawatts (TW) of photovoltaic power going directly to the grid and another 7.5 TW dedicated to compressed-air storage; 2.3 TW of concentrated solar power plants; and 1.3 TW of distributed photovoltaic installations. Supply would be rounded out with 1 TW of wind farms, 0.2 TW of geothermal power plants and 0.25 TW of biomass-based production for fuels. The model includes 0.5 TW of geothermal heat pumps for direct building heating and cooling. The solar systems would require 165,000 square miles of land, still less than the suitable available area in the Southwest.

In 2100 this renewable portfolio could generate 100 percent of all U.S. electricity and more than 90 percent of total U.S. energy. In the spring and summer, the solar infrastructure would produce enough hydrogen to meet more than 90 percent of all transportation fuel demand and would replace the small natural gas supply used to aid compressed-air turbines. Adding 48 billion gallons of biofuel would cover the rest of transportation energy. Energy-related carbon dioxide emissions would be reduced 92 percent below 2005 levels.

COURTESY OF NREL

Concentrated Solar

Large concentrated solar power plants would complement photovoltaic farms in the Southwest. The Kramer Junction plant in California's Mojave Desert (*left*), using technology from Solel in Beit Shemesh, Israel, has been operating since 1989. Metallic parabolic mirrors focus sunlight on a pipe, heating fluid such as ethylene glycol inside (*right*). The mirrors rotate to track the sun. The hot pipes run alongside a second loop inside a heat exchanger that contains water, turning it to steam that drives a turbine. Future plants could also send the hot fluid through a holding tank, heating molten salt; that reservoir would retain heat that could be tapped at night for the heat exchanger.

Who Pays?

Our model is not an austerity plan, because it includes a 1 percent annual increase in demand, which would sustain lifestyles similar to those today with expected efficiency improvements in energy generation and use. Perhaps the biggest question is how to pay for a $420-billion overhaul of the nation's energy infrastructure. One of the most common ideas is a carbon tax. The International Energy Agency suggests that a carbon tax of $40 to $90 per ton of coal will be required to induce electricity generators to adopt carbon capture and storage systems to reduce carbon dioxide emissions. This tax is equivalent to raising the price of electricity by one to two cents per kWh. But our plan is less expensive. The $420 billion could be generated with a carbon tax of 0.5 cent per kWh. Given that electricity today generally sells for six to 10 cents per kWh, adding 0.5 cent per kWh seems reasonable.

Congress could establish the financial incentives by adopting a national renewable energy plan. Consider the U.S. Farm Price Support program, which has been justified in terms of national security. A solar price support program would secure the nation's energy future, vital to the country's long-term health. Subsidies would be gradually deployed from 2011 to 2020. With a standard 30-year payoff interval, the subsidies would end from 2041 to 2050. The HVDC transmission companies would not have to be subsidized, because they would finance construction of lines and converter stations just as they now finance AC lines, earning revenues by delivering electricity.

Although $420 billion is substantial, the annual expense would be less than the current U.S. Farm Price Support program. It is also less than the tax subsidies that have been levied to build the country's high-speed telecommunications infrastructure over the past 35 years. And it frees the U.S. from policy and budget issues driven by international energy conflicts.

Without subsidies, the solar grand plan is impossible. Other countries have reached similar conclusions: Japan is already building a large, subsidized solar infrastructure, and Germany has embarked on a nationwide program. Although the investment is high, it is important to remember that the energy source, sunlight, is free. There are no annual fuel or pollution-control costs like those for coal, oil or nuclear power, and only a slight cost for natural gas in compressed-air systems, although hydrogen or biofuels could displace that, too. When fuel savings are factored in, the cost of solar would be a bargain in coming decades. But we cannot wait until then to begin scaling up.

Critics have raised other concerns, such as whether material constraints could stifle large-scale installation. With rapid deployment, temporary shortages are possible. But several types of cells exist that use different material combinations. Better processing and recycling are also reducing the amount of materials that cells require. And in the long term, old solar cells can largely be recycled into new solar cells, changing our energy supply picture from depletable fuels to recyclable materials.

The greatest obstacle to implementing a renewable U.S. energy system is not technology or money, however. It is the lack of public awareness that solar power is a practical alternative—and one that can fuel transportation as well. Forward-looking thinkers should try to inspire U.S. citizens, and their political and scientific leaders, about solar power's incredible potential. Once Americans realize that potential, we believe the desire for energy self-sufficiency and the need to reduce carbon dioxide emissions will prompt them to adopt a national solar plan. ■

MORE TO EXPLORE

The Terawatt Challenge for Thin Film Photovoltaic. Ken Zweibel in *Thin Film Solar Cells: Fabrication, Characterization and Applications.* Edited by Jef Poortmans and Vladimir Arkhipov. John Wiley & Sons, 2006.

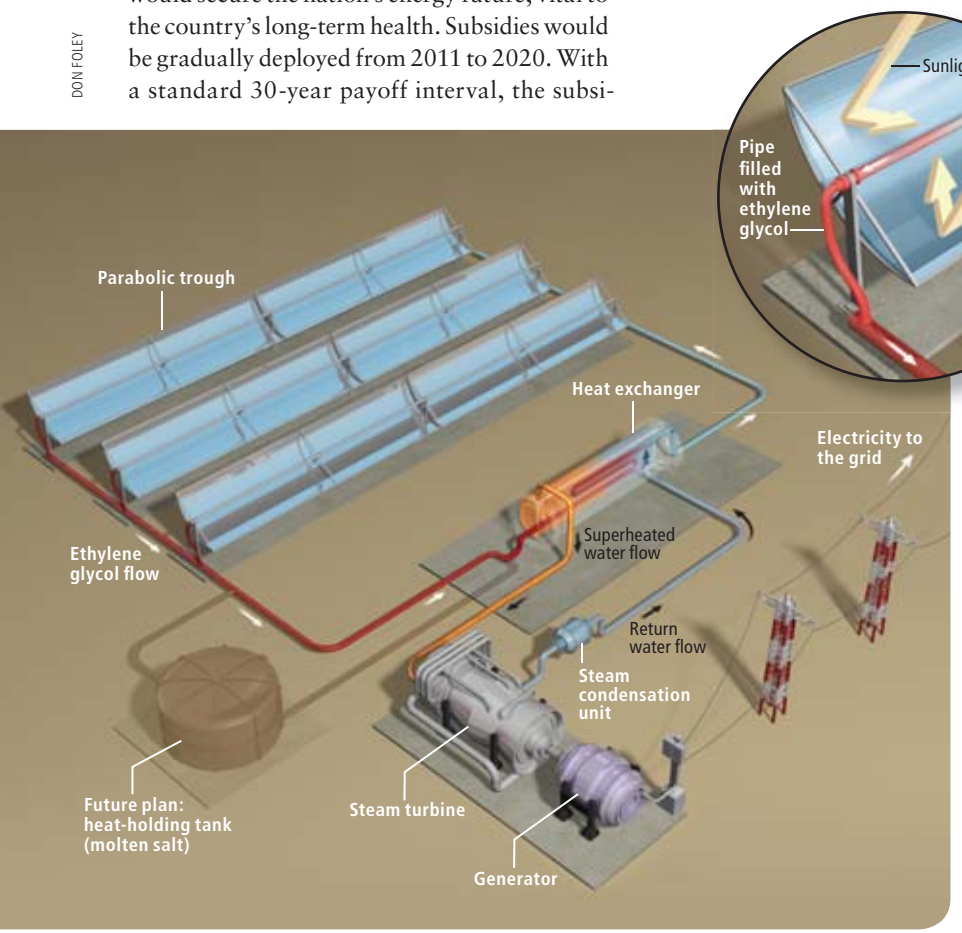
Energy Autonomy: The Economic, Social and Technological Case for Renewable Energy. Hermann Scheer. Earthscan Publications, 2007.

Center for Life Cycle Analysis, Columbia University: **www.clca.columbia.edu**

The National Solar Radiation Data Base. National Renewable Energy Laboratory, 2007. **http://rredc.nrel.gov/solar/old_data/nsrdb**

The U.S. Department of Energy Solar America Initiative: **www1.eere.energy.gov/solar/solar_america**

DON FOLEY



Second Thoughts about Fluoride

New research indicates that a cavity-fighting treatment could be risky if overused

By Dan Fagin

KEY CONCEPTS

- Researchers are intensifying their scrutiny of fluoride, which is added to most public water systems in the U.S. Some recent studies suggest that overconsumption of fluoride can raise the risks of disorders affecting teeth, bones, the brain and the thyroid gland.
- A 2006 report by a committee of the National Research Council recommended that the federal government lower its current limit for fluoride in drinking water because of health risks to both children and adults.

—The Editors

Long before the passionate debates over cigarettes, DDT, asbestos or the ozone hole, most Americans had heard of only one environmental health controversy: fluoridation. Starting in the 1950s, hundreds of communities across the U.S. became embroiled in heated battles over whether fluorides—ionic compounds containing the element fluorine—should be added to their water systems. On one side was a broad coalition of scientists from government and industry who argued that adding fluoride to drinking water would protect teeth against decay; on the other side were activists who contended that the risks of fluoridation were inadequately studied and that the practice amounted to compulsory medication and thus was a violation of civil liberties.

The advocates of fluoride eventually carried the day, in part by ridiculing opponents such as the right-wing John Birch Society, which called fluoridation a communist plot to poison America. Today almost 60 percent of the U.S. population drinks fluoridated water, including residents of 46 of the nation's 50 largest cities. Outside the U.S., fluoridation has spread to Canada, the U.K., Australia, New Zealand and a few other countries. Critics of the practice have generally been dismissed as gadflies or zealots by mainstream researchers and public health agencies in those countries as well as the U.S. (In other nations, however, water fluoridation is rare and controversial.) The U.S. Centers for Disease Control and Prevention even lists water fluoridation as one of the 10 greatest health achievements of the 20th century, alongside vaccines and family planning.

Now, though, scientific attitudes toward fluoridation may be starting to shift in the country where the practice began. After spending more than two years reviewing and debating hundreds of studies, a committee of the National Research Council (NRC) released a report in 2006 that gave a tinge of legitimacy to some longtime assertions made by antifluoridation campaigners. The report concluded that the Environmental Protection Agency's current limit

AARON GOODMAN

▲ TOO MUCH OF A GOOD THING: **Fluoride is in many foods, beverages and dental products. The ubiquity of the cavity-fighting chemical can result in overconsumption, particularly among young children.**

for fluoride in drinking water—four milligrams per liter (mg/L)—should be lowered because of health risks to both children and adults. In children, consistent exposure to fluoride at that level can discolor and disfigure emerging permanent teeth—a condition called dental fluorosis. In adults, the same fluoride level appears to increase the risk of bone fracture and, possibly, of moderate skeletal fluorosis, a painful stiffening of the joints. Most fluoridated water contains much less fluoride than the EPA limit, but the situation is worrisome because there is so much uncertainty over how much additional fluoride we ingest from food, beverages and dental products. What is more, the NRC panel noted that fluoride may also trigger more serious health problems, including bone cancer and damage to the brain and thyroid gland. Although these effects are still unproved, the panel argued that they deserve further study.

The largest long-running investigation of the effects of fluoride is the Iowa Fluoride Study, di-

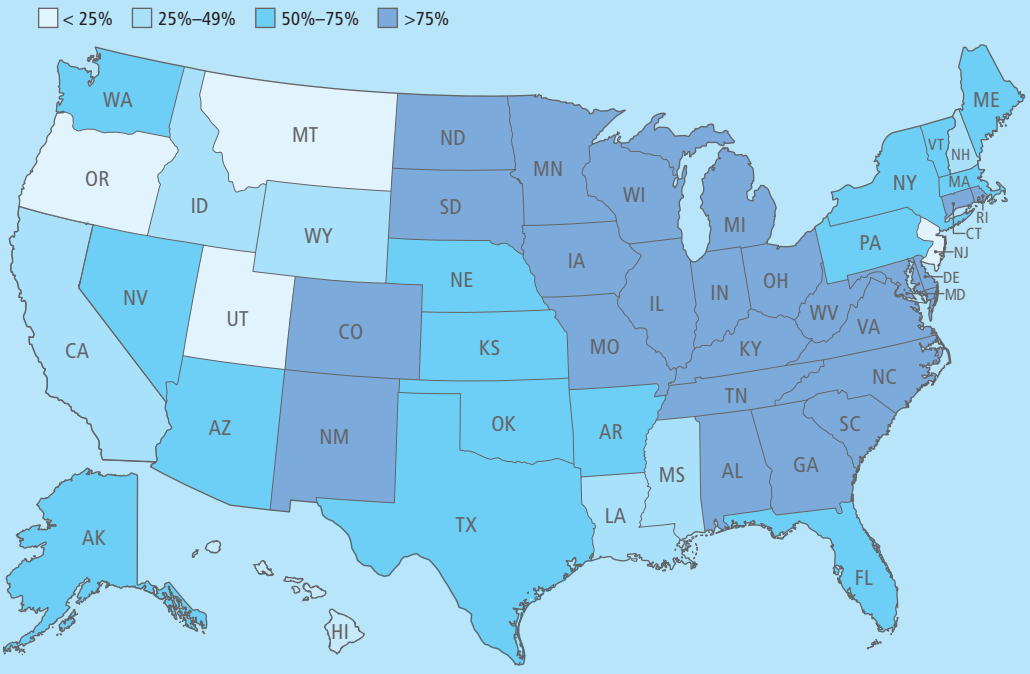
[TRENDS]

FLUORIDATION ACROSS AMERICA

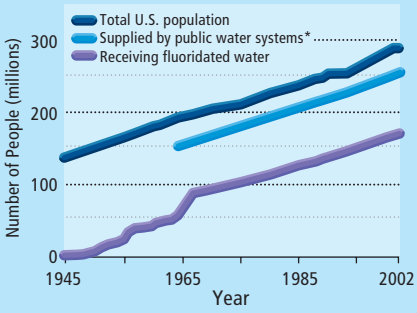
59% of the U.S. population received fluoridated water in 2002

Water fluoridation has spread across the U.S. since its introduction in 1945. In 2002, the latest year for which data are available, Americans receiving fluoridated water represented 67 percent of all people supplied by public water systems and 59 percent of the total population. Fluoridation is most prevalent in the District of Columbia (100 percent) and Kentucky (99.6 percent) and least common in Hawaii (8.6 percent) and Utah (2.2 percent).

PERCENTAGE OF STATE POPULATIONS RECEIVING FLUORIDATED WATER, 2002



FLUORIDATION RISING IN THE U.S.



*Data on public water systems not available before 1964

[THE AUTHOR]

Dan Fagin is an associate professor of journalism and director of the Science, Health and Environmental Reporting Program at New York University. A former environmental and science writer for *Newsday,* his articles on cancer epidemiology won the AAAS Science Journalism Award in 2003. Fagin is co-author of *Toxic Deception* (Common Courage Press, 1999) and is working on a book about gene-environment interactions and the childhood cancer cluster in Toms River, N.J.

rected by Steven M. Levy of the University of Iowa College of Dentistry. For the past 16 years Levy's research team has closely tracked about 700 Iowa children to try to tease out subtle effects of fluoridation that may have been overlooked by previous studies. At the same time, Levy is also leading one of the most extensive efforts ever to measure fluoride concentrations in thousands of products—including foods, drinks and toothpastes—to develop credible estimates of typical fluoride intake.

It is a maddeningly complex area of research because diets, toothbrushing habits and water fluoridation levels vary so much and also because genetic, environmental and even cultural factors appear to leave some people much more susceptible to the effects of fluoride—both positive and negative—than others. Despite all the uncertainties, however, Levy and some other fluoride researchers have come around to the view that some children, especially very young ones, are probably getting more fluoride than they should. Most of those scientists, including Levy, still support water fluoridation as a proved method of controlling tooth decay, especially in populations where oral hygiene is poor. But the researchers also believe that in communities with good dental care the case for fluoridation is not as strong as it used to be. "Instead of just pushing for more fluoride, we need to find the right balance," Levy says.

The Advent of Fluoride

Framed toothpaste advertisements from more than half a century ago hang on the walls of Levy's conference room. One touting Pebeco Toothpaste reads: "Do you want your teeth to ache and get ugly?" Another asserts that "Colgate Chlorophyll Toothpaste Destroys Bad Breath." They are artifacts of the prefluoride era, when tooth decay—called caries in the parlance of dentistry—was pervasive and toothpastes were marketed with questionable medical claims.

The introduction of fluoride changed all that. In 1945 Grand Rapids, Mich., became the first city to fluoridate its water supply. Ten years later Procter & Gamble introduced Crest, the first fluoridated toothpaste, which contained stannous fluoride (a compound with one atom of tin and two of fluorine). Colgate-Palmolive followed in 1967 by modifying its Colgate brand with what has become one of the dominant cavity-fighting ingredients in toothpastes: sodium monofluorophosphate. Instead of sticking with the fluoride salts found in toothpastes and fa-

COURTESY OF ANNA FAGIN (*Fagin*); LUCY READING-IKKANDA (*map and graph*); MOODBOARD/CORBIS (*paper clip*)

vored by dentists in office treatments, most water suppliers eventually switched to the cheaper option of fluoridating with silicofluorides such as hexafluorosilicic acid, a by-product of a fertilizer manufacturing process in which phosphate ores are treated with sulfuric acid.

By the 1970s and 1980s America was awash in various forms of fluoride, and fluoridation had become the cornerstone of preventative dentistry in most English-speaking countries. Exactly why and how much caries incidence decreased during the same period is a matter of fierce debate, but the consensus among dental researchers is that the decline was steep and that fluoride deserved much of the credit.

That was the culture in which Levy got his start in public health dentistry in the mid-1980s. Colgate-Palmolive funded his early research, which had the effect of encouraging more fluoride use in dental offices. But as American dentists began to see fewer cavities and more fluorosis on the teeth of their young patients, Levy started to wonder whether children were getting too much of a good thing. "There was a transition in my own thinking from 'more fluoride is definitely our goal' to making sure we understand where the right balance is between caries and fluorosis."

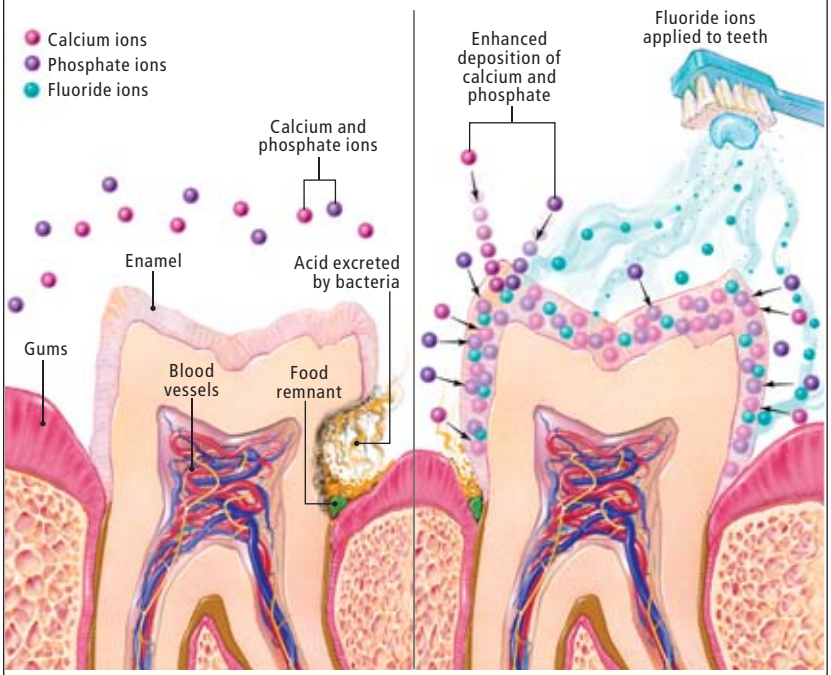
Fluoride's role in causing one disease and deterring another is rooted in the fluorine ion's powerful attraction to calcium-bearing tissues in the body. In fact, more than 99 percent of ingested fluoride that is not quickly excreted ends up in bones and teeth. Fluoride inhibits cavities through two separate mechanisms. First, fluoride that touches the enamel—the hard, white outer layer of the teeth—becomes embedded in the crystalline structures of hydroxylapatite, the main mineral component of teeth and bones. The fluorine ions replace some of the hydroxyl groups in the hydroxylapatite molecules of the enamel, and this substitution makes teeth slightly more resistant to the enamel-dissolving acid excreted by bacteria in the mouth as they consume food remnants. Second, the fluoride on the surface of teeth serves as a catalyst that enhances the deposition of calcium and phosphate, making it easier for the body to continually rebuild the enamel crystals that the bacteria are dissolving.

Fluoride has a very different effect, however, when large doses are ingested by young children whose permanent teeth are still developing and have not yet erupted. The key proteins in early tooth formation are called amelogenins, which regulate the formation of hydroxylapatite crys-

[FOCUS ON TEETH]

FIGHTING CAVITIES

Fluoride's role in combating tooth decay is rooted in the ion's powerful attraction to enamel, the hard, white outer layer of the teeth.



▲ **Without Fluoride**

The primary mineral in enamel is hydroxylapatite, a crystal composed of calcium, phosphorus, hydrogen and oxygen. When food remnants become lodged between teeth, bacteria consume the sugars and excrete lactic acid, which can lower the pH of the mouth enough to dissolve the hydroxylapatite. If the rate of dissolution is higher than the rate of remineralization—the deposition of calcium and phosphate ions from saliva onto the enamel—then cavities will form in the teeth.

▲ **With Fluoride**

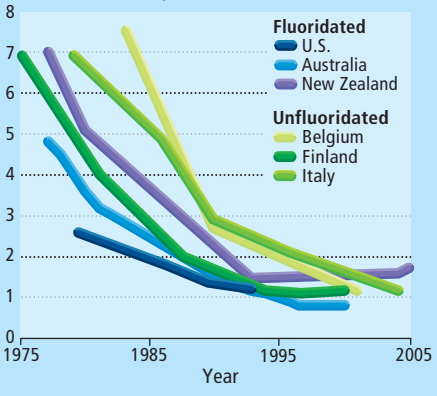
The topical application of fluoride to the teeth has two effects. First, the fluoride ions replace some of the hydroxyl groups in the hydroxylapatite molecules, creating fluorapatite crystals that are slightly more resistant to the enamel-dissolving acid excreted by the bacteria. Second, the fluoride on the surface of teeth serves as a catalyst that enhances the deposition of calcium and phosphate, thus remineralizing damaged enamel and combating decay.

Debating the Effects

The U.S. Centers for Disease Control and Prevention has hailed fluoridation as one of the 10 greatest public health achievements of the 20th century, claiming that the addition of the chemical to drinking water has been one of the main reasons for the decline in tooth decay over the past three decades (measured here by the number of decayed, missing or filled teeth in 12-year-olds). Rates of tooth decay have also plunged, however, in many countries where public water systems are not fluoridated. In some of these nations, fluoride added to foods, beverages and dental products may account for part of the decline.

TOOTH DECAY INDEX

(number of decayed, missing or filled teeth in 12-year-olds)

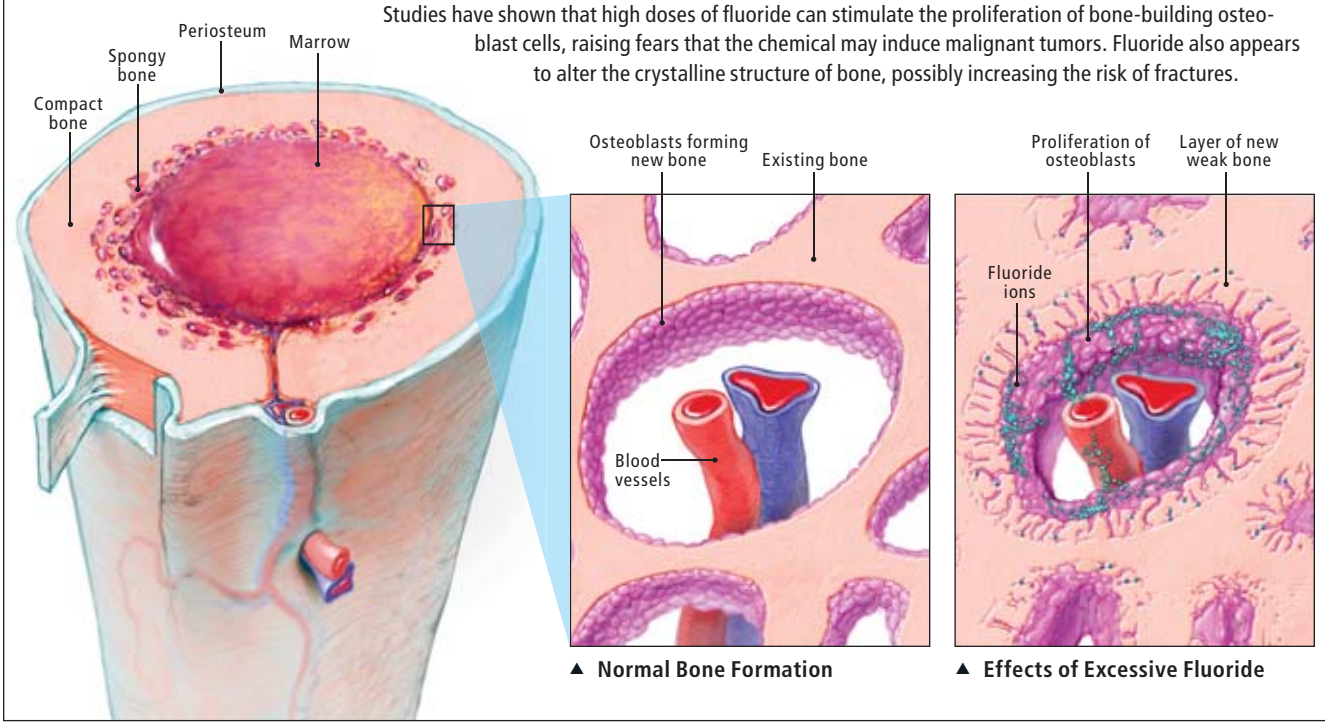


ANDREW SWIFT (*teeth*); LUCY READING-IKKANDA (*graph*)

[AREA OF CONCERN]

IS FLUORIDE WEAKENING BONE?

Scientists have focused on fluoride's effects on bone because so much of the chemical is stored there. Studies have shown that high doses of fluoride can stimulate the proliferation of bone-building osteoblast cells, raising fears that the chemical may induce malignant tumors. Fluoride also appears to alter the crystalline structure of bone, possibly increasing the risk of fractures.



▲ Normal Bone Formation

▲ Effects of Excessive Fluoride

Scientific attitudes toward fluoridation may be starting to shift in the country where the practice began.

tals. As a crystal matrix forms, the amelogenins break down and are removed from the maturing enamel. But when some children consume high doses of fluoride, which is absorbed through the digestive tract and delivered by the bloodstream to the developing teeth, the biochemical signaling goes awry and the proteins remain inside the budding tooth longer than usual, thereby creating gaps in the crystalline enamel structure. As a result, when a fluorosed tooth finally erupts it is often unevenly colored, with some portions whiter than others—a visual effect caused by light refracting off the porous enamel. In more severe cases, the surface of the tooth is pitted and the stains are brown. Nutrition and genetics can influence the risk of fluorosis, but the most important factor by far is the amount of fluoride ingested.

With grant money from the National Institute of Dental and Craniofacial Research, Levy set out to determine how much fluoride children consume and how it affects their teeth and bones. There is no universally accepted optimal level for daily intake of fluoride—that is, a level that maximizes protection against tooth decay while minimizing other risks—but the range most often cited by researchers is 0.05 to 0.07 milligram of fluoride per kilogram of body weight per day. In the early 1990s, when the children in Levy's study were infants, he found that more than a third of them were ingesting enough fluoride—mostly via water-based infant formula, baby foods and juice drinks—to put them at a high risk of developing mild fluorosis in their permanent teeth. That fraction dropped only slightly as their diet changed during their toddler years—a critical period for enamel formation in preemergent teeth. Typical fluoride ingestion stayed high during the toddler years, in part because toothpaste replaced formula as a key source. Although both children and adults are supposed to spit out their toothpaste after brushing, Levy had found in an earlier study that toddlers on average actually swallowed more than half of their toothpaste.

By the time the Iowa children were nine years old and their permanent front teeth had emerged, it was obvious that the earlier exposures to fluoride had literally left their mark. The front teeth of children who had been in the high-intake group as infants and toddlers were more than twice as likely to show the telltale staining of fluorosis than the teeth of children who had ingested less fluoride when they were younger. And as their diet broadened, so did their sources of fluoride. Tests performed in

ANDREW SWIFT

Levy's lab found, for example, that many kinds of juice drinks and soda pop contain enough fluoride (generally about 0.6 mg/L) so that drinking a little more than a liter a day would put a typical three-year-old at the optimal intake level, without counting any other daily sources.

Dozens of food items tested by Levy's team contained even higher concentrations of fluoride: an average of 0.73 mg/L in cranberry-juice cocktail, 0.71 mg/L in ice pops, 0.99 mg/L in beef gravy and 2.10 mg/L in canned crabmeat, for example. In most cases, the fluoride came from water added during processing, although higher levels also got into grapes and raisins via pesticides, into processed chicken products via ground-up bone, and into tea leaves via absorption from soil and water.

Levy found that exposure to fluoridated drinking water was an even more important risk factor for fluorosis. Iowa children who lived in communities where the water was fluoridated were 50 percent more likely to have mild fluorosis on at least two of their eight permanent front teeth at nine years of age than children living in nonfluoridated areas of the state (there was a 33 percent prevalence in the former versus 22 percent in the latter). Similar results appeared in the NRC report, which found that infants and toddlers in fluoridated communities ingest about twice as much fluoride as they should. Furthermore, the committee noted that adults who drink above-average amounts of water, including athletes and laborers, are also exceeding the optimal level for fluoride intake.

But enamel fluorosis, except in the severest cases, has no health impact beyond lowered self-esteem: the tooth marks are unattractive and do not go away (although there are masking treatments). The much more important question is whether fluoride's effects extend beyond altering the biochemistry of tooth enamel formation. Says longtime fluoride researcher Pamela DenBesten of the University of California, San Francisco, School of Dentistry: "We certainly can see that fluoride impacts the way proteins interact with mineralized tissue, so what effect is it having elsewhere at the cellular level? Fluoride is very powerful, and it needs to be treated respectfully."

Fluoride and Bone

Bone is an obvious place to look for fluoride's fingerprints because so much fluoride is stored there. What is more, studies of patients with osteoporosis—a bone disease that increases the risk of fractures—have shown that high doses of fluoride can stimulate the proliferation of bone-building osteoblast cells, even in elderly patients. The exact mechanism is still unknown, but fluoride appears to achieve this by increasing the concentrations of tyrosine-phosphorylated proteins, which are involved in biochemical signaling to osteoblasts. As with tooth enamel, however, fluoride not only stimulates bone mineralization, it also appears to alter the crystalline structure of bone—and in this case, the effects are not merely aesthetic. Although fluoride may increase bone volume, the strength of the bone apparently declines. Epidemiological studies and tests on lab animals suggest that high fluoride exposure increases the risk of bone fracture, especially in vulnerable populations such as the elderly and diabetics. Although those studies are still somewhat controversial, nine of the 12 members of the NRC panel concluded that a lifetime of exposure to drinking water fluoridated at 4 mg/L or higher does indeed raise the risk of fracture. The committee noted that lower fluoridation levels may also increase the risk, but the evidence is murkier.

As the Iowa children in his study enter adolescence, Levy hopes that analyses of the strength of their spine, hips and overall skeleton will point to possible connections between fluoride intake and bone health. He presented some preliminary data in 2007, finding little difference in the mineral content of the bones of 11-year-olds based on how much fluoride they had ingested as young children. As they go through adolescence, however, Levy thinks that trends may emerge.

The even bigger question looming over the fluoride debate is whether these known cellular effects in bones and teeth are clues that fluoride is affecting other organs and triggering other diseases besides fluorosis. The biggest current debate is over osteosarcoma—the most common form of bone cancer and the sixth most prevalent cancer in children. Because fluoride stimulates the production of osteoblasts, several researchers have suggested that it might induce malignant tumors in the expanding cell population. A 1990 study conducted by the U.S. government's National Toxicology Program found a positive dose-response relation for osteosarcoma incidence in male rats exposed to different amounts of fluoride in drinking water (all those amounts, as is typical for ani-

SIGNS OF FLUOROSIS

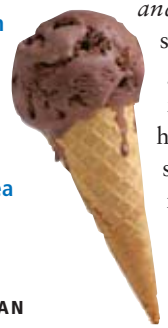
When young children consume large amounts of fluoride, the chemical can disrupt the development of their permanent teeth. When the teeth emerge, their enamel may be discolored (*top*) or, in more severe cases, disfigured (*bottom*). Researchers have found that this condition, called dental fluorosis, is more common in communities where the drinking water is fluoridated.

STEVEN M. LEVY *University of Iowa*

A FLUORIDE DIET

The optimal range for daily intake of fluoride—the level that maximizes protection against tooth decay but minimizes other risks—is generally considered to be 0.05 to 0.07 milligram for each kilogram of body weight. Consuming foods and beverages with large amounts of fluoride can put a diet above this range. Below are typical trace levels of fluoride, measured in parts per million (ppm), found in foods and drinks tested at the University of Iowa College of Dentistry.

3.73 ppm Brewed black tea
2.34 ppm Raisins ▸
2.02 ppm White wine
1.09 ppm Apple-flavored juice drink
0.91 ppm Brewed coffee
0.71 ppm Tap water *(U.S.-wide average)*
0.61 ppm Chicken soup broth
0.60 ppm Diet Coke *(U.S.-wide average)*
0.48 ppm Hot dog
0.46 ppm Grapefruit juice
0.45 ppm Beer ▸
0.45 ppm Baked russet potatoes
0.35 ppm Cheddar cheese
0.33 ppm Flour tortillas
0.32 ppm Creamed corn (baby food)
0.23 ppm Chocolate ice cream ▸
0.13 ppm Brewed chamomile tea
0.03 ppm Milk (2%)



mal studies, were far above the actual exposures found in fluoridated communities). But other animal studies as well as most epidemiological studies in human populations have been ambiguous at best.

The latest dustup over fluoride and osteosarcoma was instigated by a young researcher named Elise B. Bassin of the Harvard School of Dental Medicine. Bassin collected information about fluoride exposures among 103 osteosarcoma patients and 215 matched control subjects and concluded that fluoride is a risk factor for the cancer among boys (the results were ambiguous for girls). Bassin's report appeared in 2006 in the journal *Cancer Causes and Control;* in the same issue, however, her dissertation adviser at Harvard, Chester Douglass, wrote a commentary warning readers to be "especially cautious" in interpreting her findings because, he said, better data, still unpublished, contradict them. Antifluoridationists and some environmental groups quickly rushed to Bassin's defense, demanding that Harvard investigate Douglass, professor and chair of epidemiology at the dental school, for allegedly misrepresenting Bassin's work and for having a conflict of interest because he is editor in chief of a newsletter for dentists funded by Colgate. The university's investigation of Douglass, completed in 2006, concluded that there was no misconduct or conflict of interest.

Clashes over the possible neurological effects of fluoride have been just as intense. Phyllis Mullenix, then at the Forsyth Institute in Boston, set off a firestorm in the early 1990s when she reported that experiments on lab rats showed that sodium fluoride can accumulate in brain tissue and affect animal behavior. Prenatal exposures, she reported, correlated with hyperactivity in young rats, especially males, whereas exposures after birth had the opposite effect, turning female rats into what Mullenix later described as "couch potatoes." Although her research was eventually published in *Neurotoxicology and Teratology,* it was attacked by other scientists who said that her methodology was flawed and that she had used unrealistically high dosages. Since then, however, a series of epidemiological studies in China have associated high fluoride exposures with lower IQ, and research has also suggested a possible mechanism: the formation of aluminum fluoride complexes—small inorganic molecules that mimic the structure of phosphates and thus influence enzyme activity in the brain. There is also some evidence that the silicofluorides used in water fluoridation may enhance the uptake of lead into the brain.

The endocrine system is yet another area where some evidence exists that fluoride can have an impact. The NRC committee concluded that fluoride can subtly alter endocrine function, especially in the thyroid—the gland that produces hormones regulating growth and metabolism. Although researchers do not know how fluoride consumption can influence the thyroid, the effects appear to be strongly influenced by diet and genetics. Says John Doull, professor emeritus of pharmacology and toxicology at the University of Kansas Medical Center, who chaired the NRC committee: "The thyroid changes do worry me. There are some things there that need to be explored."

The Controversy Continues

The release of the NRC report has not triggered a public stampede against fluoridation, nor has it prompted the EPA to quickly lower its fluoride limit of 4 mg/L (the agency says it is still studying the issue). Water suppliers who add fluoride typically keep levels between 0.7 to 1.2 mg/L, far below the EPA limit. About 200,000 Americans—and several million people in China, India, the Middle East, Africa and Southeast Asia—drink concentrations higher than the limit, but their excess fluoride comes from naturally occurring runoff from fluoride-containing rocks and soils near water sources.

The report is, however, prompting some researchers to wonder whether even 1 mg/L is too much in drinking water, in light of the growing recognition that food, beverages and dental products are also major sources of fluoride, especially for young children. The NRC committee did not formally address the question, but its analyses suggest that lower water fluoridation levels may pose risks, too. "What the committee found is that we've gone with the status quo regarding fluoride for many years—for too long, really—and now we need to take a fresh look," Doull says. "In the scientific community, people tend to think this is settled. I mean, when the U.S. surgeon general comes out and says this is one of the 10 greatest achievements of the 20th century, that's a hard hurdle to get over. But when we looked at the studies that have

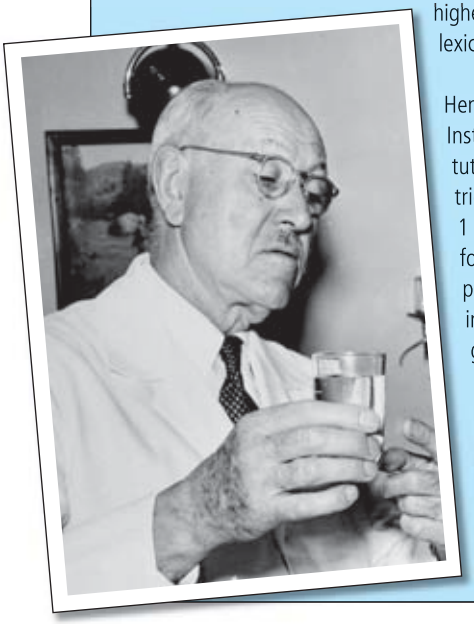
[BACKGROUND]

FLUORIDE HISTORY

The risks of fluoride were known long before its benefits. Starting in the first decade of the 20th century, a dentist named Frederick McKay traveled the American West investigating reports of what was then known as Colorado Brown Stain. With a collaborator, G. V. Black, dean of the Northwestern University Dental School, McKay discovered that children born in Colorado Springs, Colo., had stained teeth, but adults who moved there did not. They hypothesized that young children whose permanent teeth had not yet erupted or developed enamel faced the highest risk of developing the stain. McKay, who guessed that the stain was caused by some unknown compound in the local drinking water, also noticed a curious fact: the mottled teeth were surprisingly resistant to decay.

The cause remained a mystery until 1930, when McKay went to Arkansas to investigate reports of tooth staining in Bauxite, a company town owned by the Aluminum Company of America (Alcoa). Worried that aluminum might be blamed, Alcoa's chief chemist, H. V. Churchill, tested the local water and discovered something McKay had never suspected: high levels of naturally occurring fluoride. McKay quickly tested other suspect water supplies and found that wherever fluoride levels were high—typically 2.5 milligrams per liter or higher—Colorado Brown Stain was prevalent. A new disease entered the lexicon: fluorosis.

Spurred by Churchill's and McKay's discoveries, a researcher named Henry Trendley Dean, head of the dental hygiene unit at the National Institute of Health (which later changed its name to the National Institutes of Health), tried to determine how much fluoride was enough to trigger fluorosis. By the late 1930s he had concluded that levels below 1 mg/L would pose little risk. Dean remembered that McKay had found that fluorosed teeth were resistant to decay, and so he began pushing for a citywide test of a revolutionary idea: deliberately adding fluoride to water at levels that would deter cavities without triggering fluorosis. He got his wish in 1945 in Grand Rapids, Mich., and Dean went on to become fluoridation's leading advocate as the first director of the newly formed National Institute of Dental Research from 1948 until his retirement in 1953. —*D.F.*



◀ COLORADO DENTIST **Frederick McKay, whose investigations led to the discovery of fluoride's effects on teeth.**

BETTMANN/CORBIS

been done, we found that many of these questions are unsettled and we have much less information than we should, considering how long this [fluoridation] has been going on. I think that's why fluoridation is still being challenged so many years after it began. In the face of ignorance, controversy is rampant."

Some longtime fluoride researchers, however, remain unimpressed by the evidence of effects beyond teeth and bones, and they continue to push for an expansion of water fluoridation in the U.S. and elsewhere. Their view remains the official position of the American Dental Association and the U.S. Public Health Service. "We feel there are enough communities out there with high caries rates to justify additional fluoridation," says Jayanth V. Kumar, director of oral health surveillance and research at the New York State Department of Health and a member of the NRC panel who dissented from some of its findings. He acknowledges, however, that the argument for water fluoridation is not as strong in affluent areas with good nutrition and dental care. "Today it depends on what the caries level is in the community. If the disease is low, the return on investment [for fluoridation] may not be all that great."

Opponents of fluoridation, meanwhile, have been emboldened by the NRC report. "What the committee did was very, very important, because it's the first time a truly balanced panel has looked at this and raised important questions," says Paul Connett, a chemistry professor at St. Lawrence University and the executive director of the Fluoride Action Network, one of the most active antifluoridation groups worldwide. "I absolutely believe it's a scientific turning point because now everything's on the table. Fluoride is the most consumed drug in the U.S., and it's time we talked about it." ■

MORE TO EXPLORE

Patterns of Fluoride Intake from Birth to 36 Months. Steven M. Levy, John J. Warren, Charles S. Davis, H. Lester Kirchner, Michael J. Kanellis and James S. Wefel in *Journal of Public Health Dentistry,* Vol. 61, No. 2, pages 70–77; June 2001.

Patterns of Fluoride Intake from 36 to 72 Months of Age. Steven M. Levy, John J. Warren and Barbara Broffitt in *Journal of Public Health Dentistry,* Vol. 63, No. 4, pages 211–220; December 2003.

Timing of Fluoride Intake in Relation to Development of Fluorosis on Maxillary Central Incisors. Liang Hong, Steven M. Levy, Barbara Broffitt, John J. Warren, Michael J. Kanellis, James S. Wefel and Deborah V. Dawson in *Community Dentistry and Oral Epidemiology,* Vol. 34, No. 4, pages 299–309; August 2006.

Age-Specific Fluoride Exposure in Drinking Water and Osteosarcoma. Elise B. Bassin, David Wypij, Roger B. Davis and Murray A. Mittleman in *Cancer Causes and Control,* Vol. 17, No. 4, pages 421–428; May 2006.

Caution Needed in Fluoride and Osteosarcoma Study. Chester W. Douglass and Kaumudi Joshipura in *Cancer Causes and Control,* Vol. 17, No. 4, pages 481–482; May 2006.

Fluoride in Drinking Water: A Scientific Review of EPA's Standards. National Academy of Sciences, 2006. Available at **www.nap.edu/catalog.php?record_id=11571**

Self-Powered Nanotech

By Zhong Lin Wang

Nanosize machines need still tinier power plants

KEY CONCEPTS

- Nanotechnology has huge potential—but those minuscule devices will need a power source that is better than a battery.
- Waste energy, in the form of vibrations or even the human pulse, could provide sufficient power to run such tiny gadgets.
- Arrays of piezoelectric nanowires could capture and transmit that waste energy to nanodevices.
- Medical devices will likely be a major application. A pacemaker's battery could be charged so it would not need replacing, or implanted wireless nanosensors could monitor blood glucose for diabetics. *—The Editors*

The watchmaker in the 1920s who devised the self-winding wristwatch was on to a great idea: mechanically harvesting energy from the wearer's moving arm and putting it to work rewinding the watch spring.

Today we are beginning to create extremely small energy harvesters that can supply electrical power to the tiny world of nanoscale devices, where things are measured in billionths of a meter. We call these power plants nanogenerators. The ability to make power on a minuscule scale allows us to think of implantable biosensors that can continuously monitor a patient's blood glucose level, or autonomous strain sensors for structures such as bridges, or environmental sensors for detecting toxins—all running without the need for replacement batteries. Energy sources are desperately needed for nanorobotics, microelectromechanical systems (MEMS), homeland security and even portable personal electronics. It is hard to imagine all the uses such infinitesimal generators may eventually find.

Researchers are pursuing several different routes toward power generation on a miniature scale. Options include exploiting random vibrations or motions (such as those near a roadway), temperature gradients (for example, ground temperature is fairly constant several meters below the surface), biochemistry, and external energy sources such as ultrasonic waves or even audible noises.

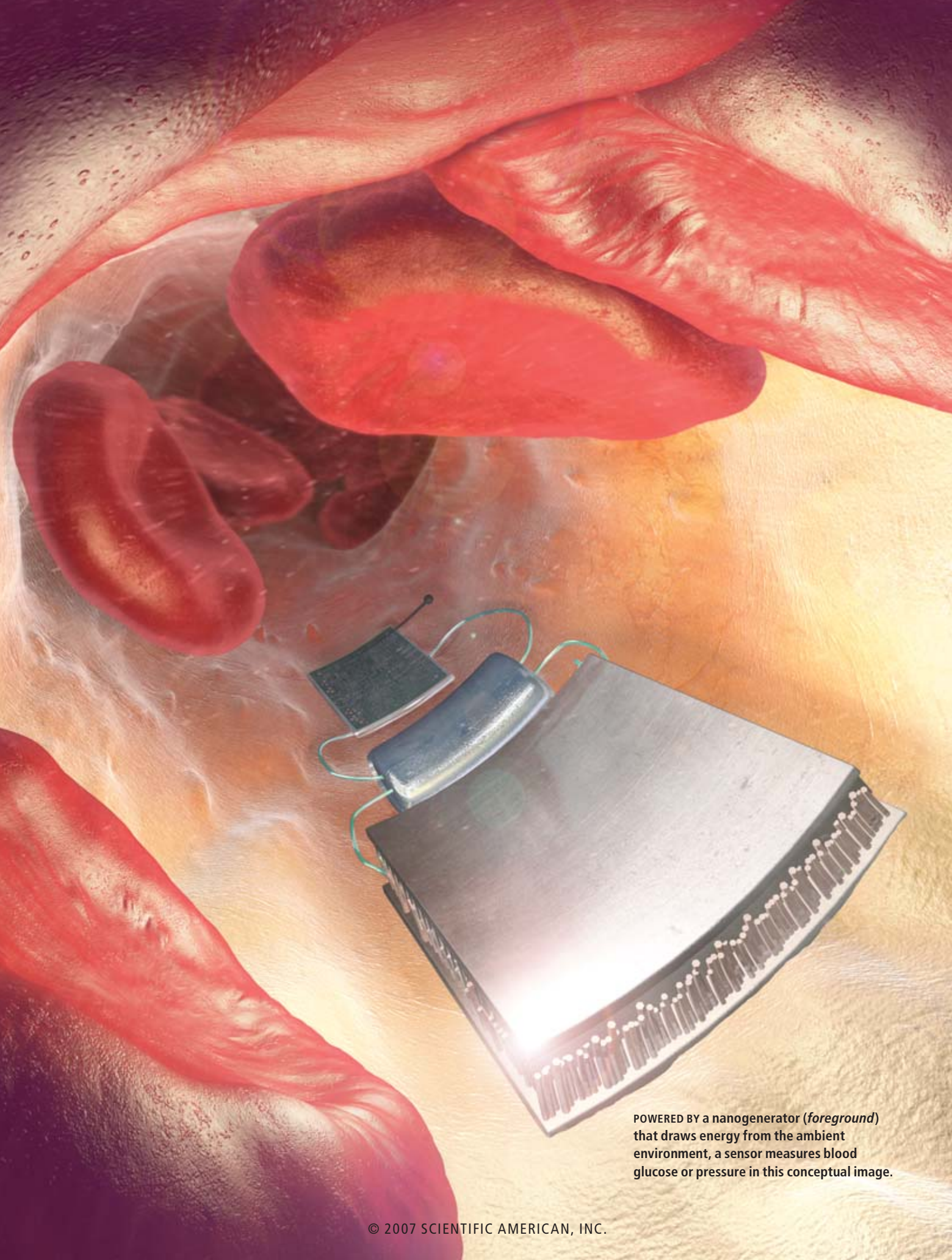
A key advantage of nanodevices and nanosystems is that they usually operate at a very low power level, in the range of nanowatts to microwatts, bringing nanogenerators for powering them into the realm of the possible. Just think of the potential power sources a human body provides: mechanical energy, heat energy, vibration energy, chemical energy (in the form of glucose) and the hydraulic energy of the circulatory system. Converted into electricity, just a small fraction of this energy could be sufficient to power many types of small devices [*see box on page 86*].

Power to the Tiny

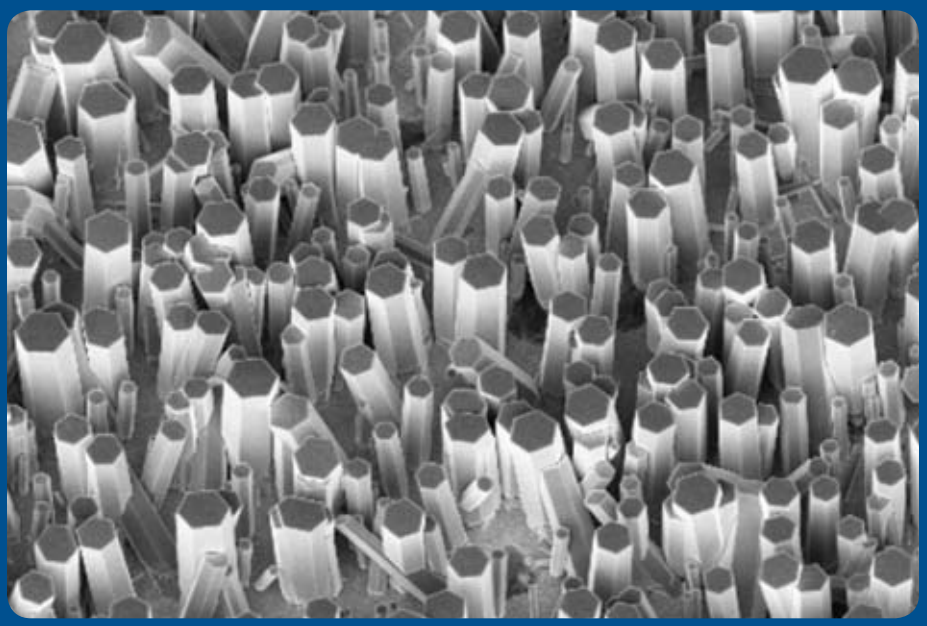
Work on power generation for small devices has moved quickly since the late 1990s, when the proliferation of portable electronic gadgets attracted researchers to the problem of finding new ways to power them. Experimenters at the Massachusetts Institute of Technology's Media Lab, for example, devised an energy-scavenging shoe using the piezoelectric effect, whereby certain crystalline materials produce a voltage when mechanically stressed. But the difficulty of producing useful amounts of power soon drove scientists to explore generators that could meet the much smaller electrical power needs of MEMS. These silicon-based devices, whose dimensions are measured in microns (millionths of a meter) to millimeters (thousandths of a meter), have found many uses, including as accelerometers for automobile air-bag systems and as ink-jet printer nozzles. Biology and chemistry also offer opportunities for producing power [*see box on page 87*].

In recent years, scientists have built small vibration-based generators using both piezoelectric and electromagnetic transducers. The electromagnetic microgenerator utilizes a moving mag-

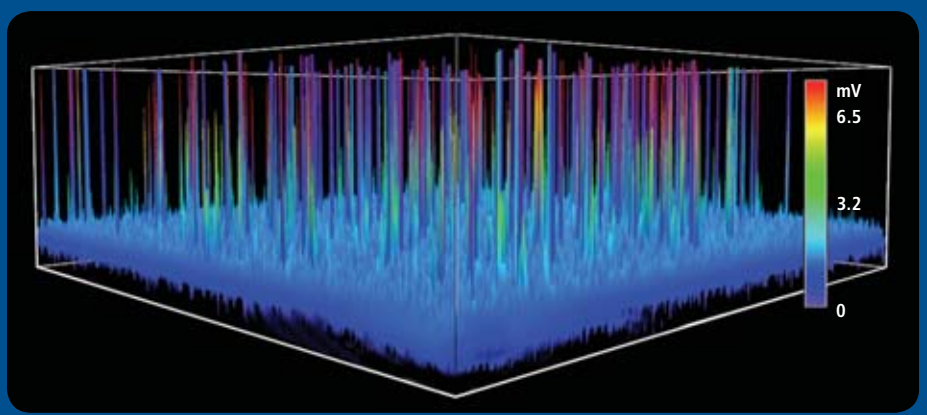
ADAM QUESTELL



POWERED BY a nanogenerator (*foreground*) that draws energy from the ambient environment, a sensor measures blood glucose or pressure in this conceptual image.



ZINC OXIDE NANOWIRES, typically 30 to 100 nanometers in diameter and one to three microns in length, are seen in this scanning electron microscope image (*above*). The voltage output in millivolts of an array shows variability (*below*).



net or coil for inducing an alternating electric current in a circuit. Although some microgenerators have been fabricated at the scale of MEMS, the technology tends to require structures ranging from one to 75 cubic centimeters, which work in vibration ranges from 50 hertz (cycles per second) to five kilohertz. A typical piezoelectric vibration-based generator uses a two-layered beam of lead zirconium titanate, with a mass located at its unsupported end, somewhat like a swimmer poised at the end of a diving board. When gravity causes the beam to bend downward, the upper piezoelectric layer is under tensile strain and the lower layer is under compressive strain. The result is a positive and negative voltage across the beam. As the mass oscillates back and forth, an alternating voltage is created. But because this energy generator is relatively large, gravity is important in driving its oscillating mass.

Now my research group at the Georgia Institute of Technology is working on piezoelectric power generation at the nanoscale. And at the nanoscale, things change. Gravity, which plays such a critical role in the larger world, is a very minor actor in the nanoworld as compared with the forces of chemical bonding and intermolecular attraction.

Where Gravity Doesn't Matter

The force of gravity is not available to us on a useful scale in the nanoworld. If one attempted to construct a piezoelectric generator with a nanometer-scale beam, gravity would make almost no contribution to sustaining the beam's motion, and the device would not work. There-

COURTESY OF ZHONG LIN WANG

[THE AUTHOR]

Zhong Lin Wang is director of the Center for Nanostructure Characterization at the Georgia Institute of Technology. He discovered the nanobelt in 2000 and the world's smallest balance, the nanobalance, in 1998. Among his many honors, he received the 1999 Burton Medal of the Microscopy Society of America.

fore, we need another method to build a nanosize generator for powering autonomous devices. Our team has been exploring innovative nanotechnologies for converting mechanical energy (such as body movement and muscle stretching), vibration energy (such as acoustic and ultrasonic waves) and hydraulic energy (such as the flow of blood and other bodily fluids) into electric energy to power nanodevices.

My research focused on carbon nanotubes in the late 1990s. We invented a few techniques for measuring the mechanical, electrical and field-emission properties of individual carbon nanotubes using in situ microscopy. But we could not control a nanotube's electrical properties. I immediately realized that metal oxides are a new world—and why not explore those nanostructures? In 2000 I started with nanobelts, white woollike products made by baking a metal oxide such as zinc in the presence of argon gas at 900 to 1,200 degrees Celsius, and with nanowires.

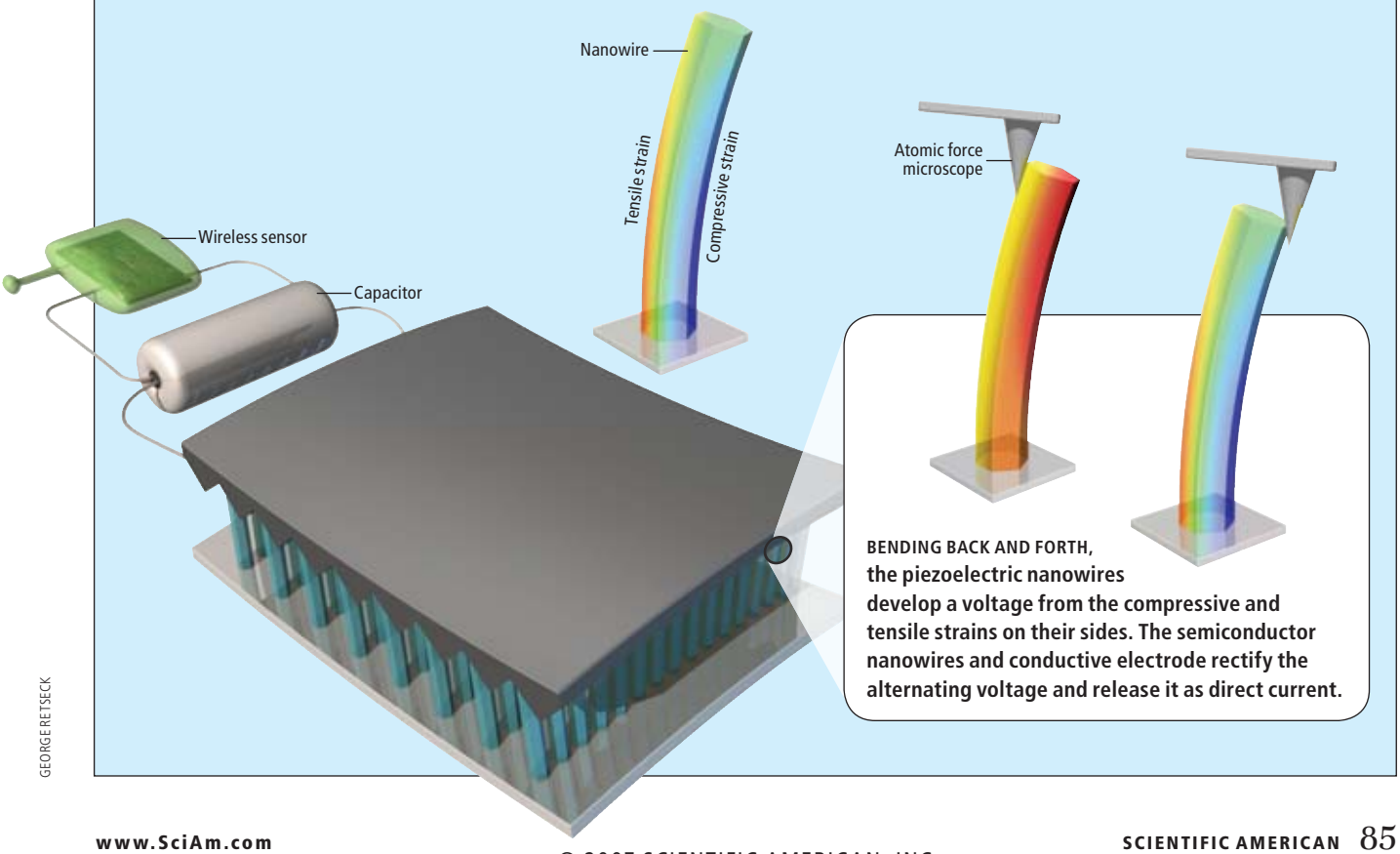
Our research has become focused on aligned zinc oxide nanowires, each of them a perfect six-sided, columnlike crystal that is grown on a solid conductive substrate using a standard vapor-liquid-solid process in a small tube furnace. We deposit gold nanoparticles, which serve as catalysts, on a sapphire substrate. An argon gas carrier flows through the furnace as a zinc oxide powder is heated. The nanowires then grow underneath the gold particles. The typical diameter of the nanowires is 30 to 100 nanometers, and they measure one to three microns in length.

The idea of converting mechanical energy into electricity came to my mind around August 2005, when we were measuring the electromechanical coupled properties of the wires. Using an atomic force microscope (AFM), we observed some voltage output peaks, but we were not sure what they were. We did systematic work through November of that year and learned that the voltage was from the piezoelectric effect of the zinc oxide; our results excluded the contribution from friction, contact or

[THE BASICS]

MECHANICAL ENERGY TO ELECTRICITY

A nanogenerator (*below left*) consists of an array of vertical zinc oxide nanowires, hexagonal crystals with both piezoelectric and semiconducting properties. A rectangular electrode with a ridged underside sits atop the nanowires and moves side to side in response to external forces such as vibration, the human pulse or acoustic waves. In this example, the generator's output is stored in a capacitor and periodically sent to a sensor, which could be measuring blood glucose or pressure. A tiny radio-frequency transmitter reports the results.



BENDING BACK AND FORTH, the piezoelectric nanowires develop a voltage from the compressive and tensile strains on their sides. The semiconductor nanowires and conductive electrode rectify the alternating voltage and release it as direct current.

GEORGE RETSECK

other confounding artifacts. The next step was determining what the process was for the charge output from a single nanowire. After studying a book on semiconductor devices, I proposed the working mechanism of what would become the nanogenerator.

Zinc oxide has the rare attribute of possessing both piezoelectric and semiconducting properties, which we put to use in creating and accumulating piezoelectric charges in the nanowires. We have shown that when the conductive tip of an AFM bends a straight, vertical nanowire, a strain field is established, with the stretched surface showing positive strain and the compressed surface showing negative strain. As the tip scans over the top of the zinc oxide nanowires, we observe many peaks in the corresponding voltage output image for each contact position [*see box on page 84*]. The piezoelectric effect creates an electric field inside the nanowire's volume, with the stretched and compressed sides of the wire showing positive and negative voltages.

The idea came first, but we needed experimental support. Just before Christmas 2005, I designed an experiment to visualize directly the voltage output of a large wire under optical and AFM microscopy. My student and I did the experiments, and one evening in late December, we were rewarded with several videos that directly proved my model. The next day I worked with Jinhui Song in my office to edit the movie. Then we sent the paper to *Science* for publication.

To be useful in practical applications, our nanogenerator needs to contain an array of nanowires, all of them continuously generating electricity that can be collected and delivered to a device. And the energy to be converted into electricity has to come in the form of a wave or vibration from the environment so the nanogenerator can operate independently and wirelessly. We have developed a novel design that addresses these requirements.

The next challenge was to increase the power of the nanogenerator. Three objectives have to be achieved: eliminate the use of the AFM, make many nanowires generate electricity simultaneously and continuously, and excite the nanowires in an indirect wave, such as an ultrasonic wave. I came out with a new design using a ridged electrode to replace the AFM tips and presented the idea to my postdoctoral assistant, Xudong Wang. It took him about four months of experiments before compiling the first group of data. The signal was rather small. From May to October 2006 we focused on the optimum packaging of the nanogenerator to enhance its output. By the end of the year we realized that the nanogenerator could at last be reported to the scientific community.

Our experimental setup provided the first demonstration of continuous direct current produced by a piezoelectric nanogenerator. It consists of an array of parallel zinc oxide nanowires and a platinum-coated silicon electrode with a ridged surface in place of the microscope's tip. Coating the electrode with platinum both enhances its conductivity and causes it to act like a diode that allows current to flow in only one direction, from metal to semiconductor. The electrode is placed above the nanowire array at a controlled distance and can be moved laterally so that it bends the nanowires from side to side. Thanks to its surface ridges, the electrode acts like an array of aligned microscope tips [*see box on preceding page*].

Flexible Future

Since January 2007 we have been fully involved in improving our nanogenerator. The ceramic or semiconductor substrates that we initially used for growing zinc oxide nanowires are hard and brittle, for instance, making them unsuitable for applications that require a foldable or flexible power source, such as biosensors implanted in muscles or joints, or power generators built into shoes.

Here is where conductive polymers can provide a substrate that is likely to be biocompatible. In experiments we discovered that many available flexible plastic substrates are suitable for growing the zinc oxide nanowire arrays, which ultimately could find applications in portable and flexible electronics. Because of the flexibility of the substrate, the nanowire surface profile was wavy, causing some missed contacts. We believe that providing suitable bonding strength between the nanowires and substrate as well as optimizing the wire spacing will be important in increasing discharge efficiency.

Although our approach has demonstrated the principle of the nanogenerator, we must drastically improve its performance to make it practical. All the nanowires must generate electricity simultaneously and continuously, and all the electricity must be effectively collected and distributed. A large-scale method for growing zinc oxide nanowires can be cost-effective because it does not require expensive high-temperature manufacturing processes. Hurdles that lie ahead

Just How Much Energy Does Your Body Produce?

Blood flow
0.93 watts of mechanical energy
0.16 W electrical energy available
0.16 joules of electrical energy per movement

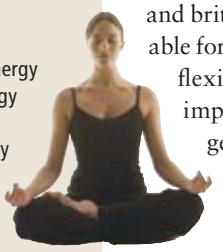
Exhalation
1.00 W mechanical energy
0.17 W electrical energy available
1.02 J electrical energy per movement

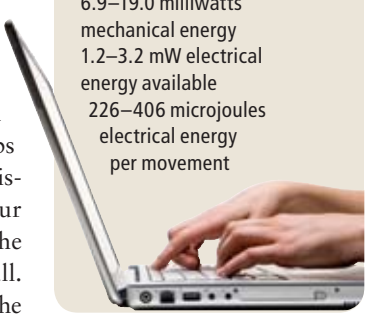
Inhalation
0.83 W mechanical energy
0.14 W electrical energy available
0.84 J electrical energy per movement

Upper limbs
3.00 W mechanical energy
0.51 W electrical energy available
2.25 J electrical energy per movement

Walking
67.00 W mechanical energy
11.39 W electrical energy available
18.90 J electrical energy per movement

Fingers typing
6.9–19.0 milliwatts mechanical energy
1.2–3.2 mW electrical energy available
226–406 microjoules electrical energy per movement





TIM PLATT *Getty Images (yoga pose)*; PM IMAGES/GETTY IMAGES *(typing on laptop)*

[OTHER IDEAS]

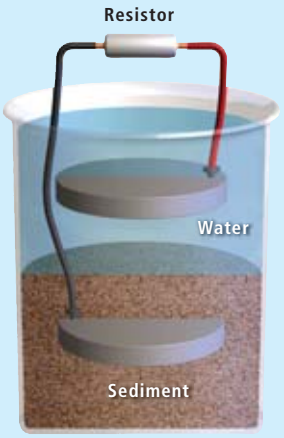
Ambient-Energy Harvesters

Nanogenerators that use vibration-driven piezoelectrics show promise, but other ways to siphon energy from the environment also exist

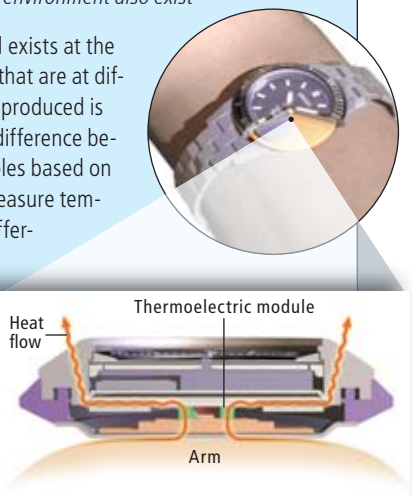
The most effective energy-harvesting processes are in nature, such as in microorganisms that must perform this task to survive. Derek R. Lovley of the University of Massachusetts Amherst and his colleagues, for instance, have reported that a marine organism, *Desulfuromonas acetoxidans,* can transfer electrons to a graphite electrode from acetate produced in sea sediments by other organisms. The result is an electric current that flows through water to another electrode. Such "sediment batteries" might be used for bioremediation of toxic wastes, for example. Similarly, the catalytic action of microorganisms can produce electrical output from different carbohydrates and substrates.

In 2004 a group of researchers led by A. K. Shukla of the Central Electrochemical Research Institute in India demonstrated biological fuel cells that use organic substances and metabolic processes to generate current. It is possible to tap into the body's own resources, including the metabolic properties of our cells, to generate enough energy to power an array of medical devices, including drug delivery systems, cardiac pacemakers and diagnostic devices. The drawback of microbial fuel cells is that their size is rather large and their power output may not be adequate for nonbiological applications.

Another option, a thermoelectric generator, relies on the Seebeck effect, wherein an electric potential exists at the junction of two dissimilar metals that are at different temperatures. The voltage produced is proportional to the temperature difference between the two ends; thermocouples based on this principle are often used to measure temperature. When a temperature difference is applied, charge carriers in the material diffuse from the hot side to the cold side. Mobile charge carriers migrating to the cold side leave behind their oppositely charged and immobile nuclei at the hot side, giving rise to a thermoelectric voltage.



SEDIMENT battery is powered by marine organisms.



THERMOELECTRIC generator exploits temperature differences.

Thermoelectrics is an exciting field, but the generators are fairly large because of the need to maintain an appreciable temperature difference between the two ends of the device. Consequently, thermoelectric generators may have limited applications as power sources that can be integrated into nanosystems. Yet they have already found some commercial applications, such as the Seiko Thermic wristwatch, introduced in 1998, which used thermoelectric modules to generate sufficient microwatts to run its mechanical workings from the small gradient between the wearer's body heat and the ambient temperature.

—Z.L.W.

in our research include learning how to grow perfectly uniform arrays of nanowires that all produce electricity and how to extend their working life. The lifetime of the current nanogenerator is about 50 hours. The main reason for the device's failure is likely the packaging technology for assembling the top electrode and the nanowire arrays. If the electrode presses on the nanowires too firmly, for example, no current will be generated. We are working hard to improve the packaging.

The process used to produce the arrays involves evaporating a thin layer of gold onto the substrate, where it acts as a catalyst for nanowire growth. The zinc oxide crystals look something like a forest without branches. To improve the adhesion of the nanowires with the substrate, we have added a thin layer of polymer onto the substrate after growth so that the roots of the nanowires are partially embedded. We have achieved electrical output of about 10 millivolts and 800 nanoamperes from a nanogenerator that is about six square millimeters in size. We have also shown that nanogenerators can be arranged in series to improve the output voltage and in parallel to improve the output current, as is commonly done with power sources such as batteries or fuel cells. But to produce higher voltages, we need to make nanowires with identical height and diameter.

Nanogenerators may never power our homes or even our flashlights; the amount of power available from them will be quite small. But nanowire arrays can be ideal generators for devices that need to work only intermittently, such as sensors that collect and transmit data for one second of every minute. In the years to come, nanogenerators will be used to harvest and recycle the energy wasted in our daily life, such as that created by pressure changes in a car tire, a moving vehicle's mechanical vibration or even the fluttering surface of a camper's tent. Consider how many small energy resources are all around us. ■

MORE TO EXPLORE

Direct-Current Nanogenerator Driven by Ultrasonic Waves. Xudong Wang, Jinhui Song, Jin Liu and Zhong Lin Wang in *Science,* Vol. 316, pages 102–105; April 6, 2007.

Nanowire Piezoelectric Nanogenerators on Plastic Substrates as Flexible Power Sources for Nanodevices. Pu Xian Gao, Jinhui Song, Jin Liu and Zhong Lin Wang in *Advanced Materials,* Vol. 19, pages 67–72; 2007.

Zhong Lin Wang's Web site is available at **www.nanoscience.gatech.edu/zlwang**

GEORGE RETSECK

LAVA erupting from an active volcano in Hawaii comes from a hotspot, akin to a flame burning through the earth's crust.

RENE FREDERICK *Getty Images*

HOT

By John A. Tarduno

Where was the cone? We had just pulled up our drill pipe, replaced its worn drill bit, and lowered it back down to the seafloor, a mile under our ship. Crowding into the control room, we watched images from a camera attached to the end of the pipe, looking for a cone we had left as a marker to guide the pipe back to the hole we were drilling. The team had gone through this exercise many times before. Usually we would see a fish swim by or a squid momentarily grab the pipe, and then the cone would appear. This time we saw only fish and squid. What had gone wrong?

We had come to the northwestern Pacific Ocean to extract core samples from the submerged extinct volcanoes, known as the Emperor seamounts, that form the northernmost leg of the Hawaiian-Emperor volcanic chain. The neat pattern formed by the chain is apparent on any world map and, along with the jigsaw-puzzle shape of South America and Africa, has long stood as a testament to plate tectonics—the principle that our planet's surface is an ever shifting mosaic of rocky puzzle pieces. Not only do the islands and seamounts form an uncannily straight line for 3,500 kilometers across the Pacific, their rocks get steadily older as you move northwest up the chain: from the Big Island (which is still growing) through Maui, Oahu, Kauai and on up to the Midway atoll, whose long-extinct volcano has subsided so much that it barely sticks up above the sea surface. Past Midway, the line makes a sharp bend, continuing northward along the Emperor seamounts and stretching

SPOTS Unplugged

Long considered fixed founts of molten material from deep within the planet, hotspots now join the list of moving parts

nearly as far as the tip of the Aleutian Islands.

The standard explanation for this pattern, based on ideas put forward by geophysicist J. Tuzo Wilson in 1963, is that the islands record motion of the Pacific plate over a volcanic hotspot [see "Hot Spots on the Earth's Surface," by Kevin C. Burke and J. Tuzo Wilson; SCIENTIFIC AMERICAN, August 1976]. The hotspot can be thought of as a candle within the earth whose flame burns through the crust, pumping lava to the surface and building an island. The ever moving plate pulls the island off the hotspot, the hotspot generates a new island, and the cycle continues. Together the hotspot and plate tectonics produce islands like an assembly line.

In 1971 Jason Morgan of Princeton University went a step further. He proposed that the "candle" was the molten tip of a plume of hot rock rising from deep within the earth's mantle. Pinned down in the planet's interior, the hotspot itself did not move; only the plate did. In this view, the Hawaiian hotspot has remained at a latitude of about 19 degrees north, while the Pacific plate has moved northwest at about 10 centimeters a year. The great bend in the hotspot's track suggests that the direction of plate motion suddenly changed some 47 million years ago.

Beyond accounting for the evolution of Hawaii and other island chains, the fixed position of hotspots has given earth scientists a very powerful set of landmarks. These landmarks have allowed geologists to reconstruct plate motions and determine the original location of geologic samples, such as sediment cores used to measure past climate and rocks used to gauge the motion of the solid earth relative to the planet's spin axis. So it has come as a shock to geologists that hotspots may not be all they appear to be.

My colleagues and I have recently demonstrated that they are not, in fact, fixed. In a sense, they are like the cone we left at the bottom of the Pacific as a reference marker. When we failed to find it in place, we realized that ocean currents must have swept it away. The team repositioned the ship, located the drilling hole, and entered it without a cone to guide us. Similarly, geophysicists now have to figure out why hotspots drift and have to develop a new way to get our bearings.

Magnetic Filings

The evidence that clinched the case for plate tectonics in the 1960s, and that has since refined our understanding of hotspots, is the record of plate movement provided by rock magnetization. When lava cools, magnetic minerals within it, principally magnetite and titanomagnetite, crystallize. These miniature bar magnets lock in the direction of the earth's magnetic field at that moment in time and that location on the surface.

Because the earth's magnetic field varies in both time and space, rock magnetization provides two ways to determine how plates have moved. First, geologists can study the time variation. At irregular time intervals, the planet's field reverses polarity: the North and South magnetic poles switch places. Consider what that means for lava erupting at mid-ocean ridges. When the rock emerges and cools, the magnetization of its

KEY CONCEPTS

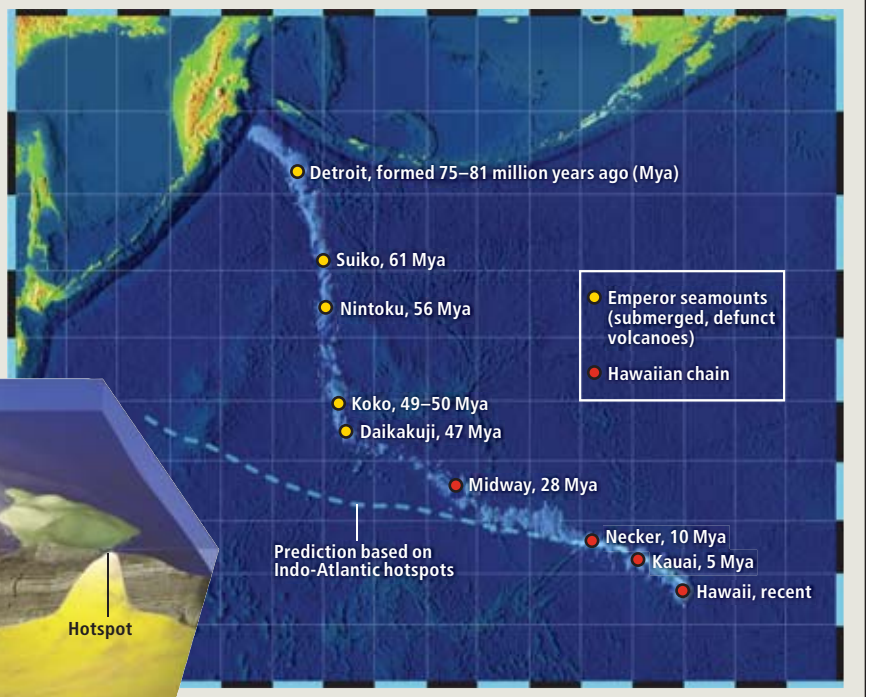
- Volcanic hotspots, such as the one creating the Hawaiian Islands today, have long been considered fixed points in the scheme of slowly moving tectonic plates that form the earth's outer surface.
- New evidence that hotspots can instead be mobile comes from study of Hawaii's chain of islands and submerged defunct volcanoes. The chain's elbowlike geometry has traditionally been attributed only to a change in the motion of the Pacific plate. Now it is in part credited to hotspot migration, itself an expression of movement in the earth's mantle deep below the surface.
- Implications include textbook rewrites, as well as new views on paleoclimate records and the stability of the entire earth on its spin axis.

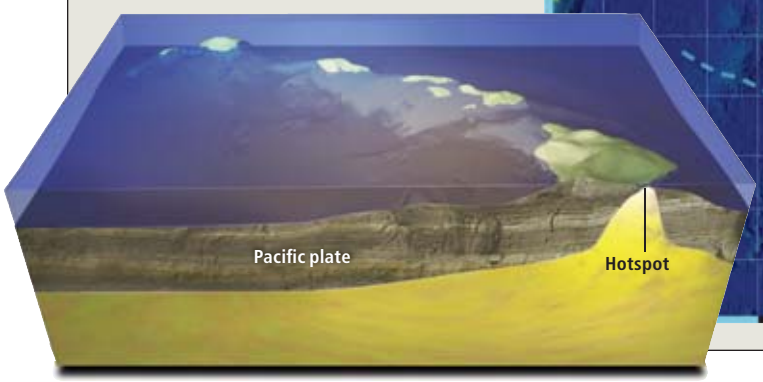
—The Editors

[CASE STUDY]

THE OLD VIEW OF HAWAII'S ORIGIN

Textbooks say that the chain composed of Hawaii's islands and the Emperor seamounts (*right*) formed as the Pacific tectonic plate passed over a fixed hotspot. Venting lava built an island; then the plate carried the island to the northwest, to be replaced by another (*below*). The chain's sharp bend was ascribed to a shift in plate motion. But varied findings indicate the scenario is incomplete. If it were correct, for instance, the chain geometry would match that predicted by the study of hotspots in the Indian and Atlantic basins (*dashed line*).





minerals lines up like magnetic filings pointing, say, to the north. Plate tectonics then carries the rocks away from the ridge. After several hundred thousand years or so, the polarity flips, and from that moment newly formed rocks are magnetized the opposite way. These, too, are carried away from the ridge. The polarity eventually flips back, and the cycle continues. The result is a series of horizontal stripes recorded in the oceanic crust, alternating between north-pointing and south-pointing magnetic minerals—a geologic version of tree rings. Geologists date the stripes by matching them against the timeline of polarity reversals. They then use time and distance data to calculate a plate's direction and speed relative to an adjoining plate.

The second technique exploits the fact that the direction of the earth's magnetic field has two components: horizontal (declination) and vertical (inclination). When you rely on a compass to find the direction of north, you use the declination, but if you look closely at the compass needle, you will see that it is also tilted slightly with respect to the horizontal. As Neil Opdyke of the University of Florida demonstrated in a classic study in the late 1960s, the inclination is directly related to latitude. Measuring inclination reveals the latitude where the rock originally formed and hence the minimum distance that the plate must have moved since then. (It does not reveal the longitude.)

Using these approaches is not entirely straightforward. The earth's magnetic field does not point purely north-south. It has a more complex shape that geophysicists think reflects the flow of liquid iron in the planet's core. When averaged over several millennia, however, these deviations cancel out. Thus, researchers can compensate for the complexity of the field by sampling a large number of rocks representing a long enough span of time. Few islands still have old rocks that date back far enough, so geologists have to drill into the ocean floor.

That process presents its own complications. Oceanic crust can be tilted, which can be mistaken for magnetic inclination. The best rock samples come from areas that seismic data confirm lie flat. Geologists have drilled deeply into only a few of these areas. Another approach is to tow a magnetometer behind a ship and measure the magnetization of the seafloor rock remotely. Unfortunately, such measurements reflect not only the magnetization imprinted when the rock formed but also the induced magnetizations imparted by the earth's present-day field, as well as the magnetization acquired over geologic time as some of the magnetic domains within the crystals spontaneously reoriented themselves.

[THE AUTHOR]

John A. Tarduno is thankful that only a single sandstorm struck his expedition to northeastern Mauritania last year. He had gone to the Sahara to recover 200-million-year-old rocks, whose ancient magnetic signatures reveal how the earth's plates have moved over the eons. Then he hauled his drilling equipment up 800-foot cliffs on Chatham Island off New Zealand, this time to obtain 85-million-year-old rocks. The North Pole and South Africa have also been on his recent itinerary. Tarduno is a professor in the departments of earth and environmental sciences and of physics and astronomy at the University of Rochester and is founder of its paleomagnetism laboratory.

COURTESY OF JOHN A. TARDUNO (*Tarduno*); KEVIN HAND (*illustration*)

Magnetometer readings therefore still need to be calibrated against directly sampled rocks.

Wide Latitude

The first hint that the Hawaiian hotspot might not be fixed came in the early 1970s from studies conducted by Tanya Atwater and Peter Molnar, both then at the Massachusetts Institute of Technology. They looked at two phenomena to deduce plate motion: seafloor stripes and island chains. When two plates meet at a mid-ocean ridge, their motions create a series of seafloor stripes and, if each plate is underlain by a hotspot, a pair of island chains. Researchers can predict what the hotspot track of an island chain should look like on one plate by examining the track of the corresponding chain on the other plate.

Atwater and Molnar reported that the predictions for several hotspot tracks failed to match the location of the actual volcanoes, suggesting that the hotspots had moved. The technique has since been refined and extended by Joann Stock of the California Institute of Technology and her colleagues, with essentially the same results. Predictions for the Hawaiian-Emperor chain made using hotspots in the Atlantic Ocean are in rough agreement with the portion of the chain formed over the past 30 million years, but they deviate further back in time. At 60 million years ago the offsets are very large.

These conclusions did not convince many geologists, however. Other effects could explain the disagreement between the two data sets. The Pacific and Atlantic basins consist of plates that abut the continent of Antarctica, which itself is made of at least two plates. These plates can rotate like interlocking gears, potentially changing the way that geographic features in the Atlantic relate to those in the Pacific. Unfortunately, much of the geologic history of Antarctica remains a mystery, buried under thick ice caps. This uncertainty prevented geologists from reconstructing the plate motions fully.

The only way to settle the matter was to go back to the rock samples. My University of Rochester colleague Rory Cottrell and I took up this challenge in 1995. We visited the Ocean Drilling Program (ODP) at Texas A&M University and examined archived cores of sediment and rock collected over several decades. The most promising had been collected in 1992 from one of the Emperor seamounts, known as Detroit, which formed between 75 million and 81 million years ago. The rock type was basalt—similar to that erupting on Hawaii's Big Island today—which carries the best-understood type of magnetic signal. The core had drawn little attention because researchers thought it was too short in length to provide enough accurate readings of magnetic inclination.

A new analysis proved otherwise. To remove the effects of induced magnetization and spontaneous reorientation of large magnetic mineral domains so that we could identify the minerals' original magnetization, we measured the samples in a shielded superconducting quantum interference device (SQUID) magnetometer and went through an exhaustive demagnetizing procedure. It turned out that the core was just long enough to provide precise readings of magnetic inclination and hence the latitude at which the minerals formed: 36 degrees north.

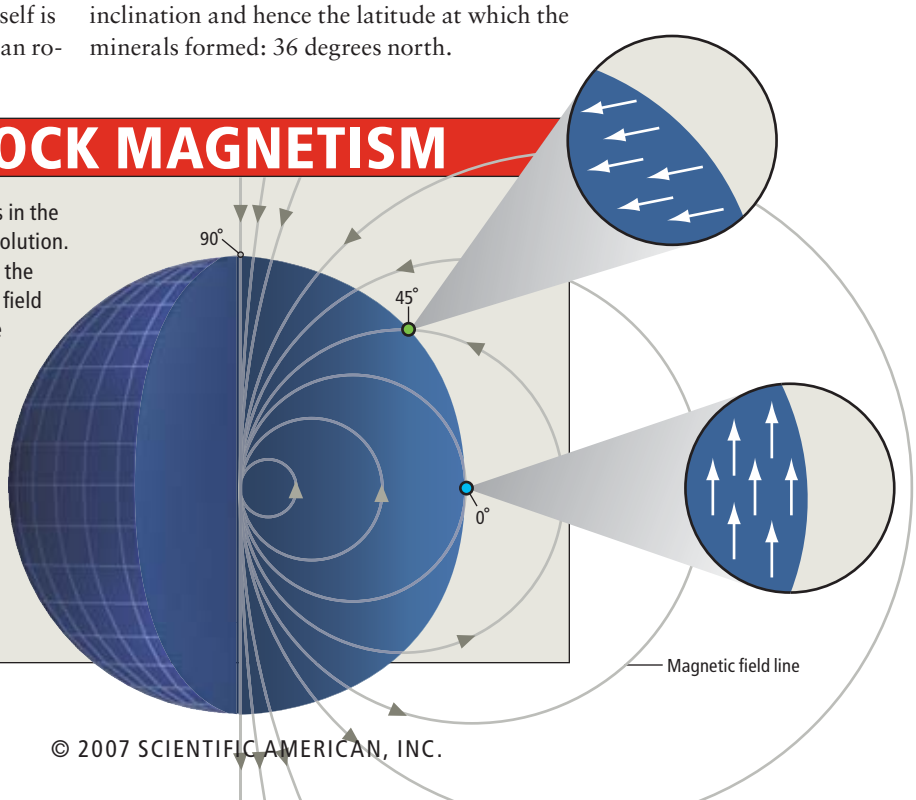
▲ **DRILL RIG towering over the deck of the *JOIDES Resolution* lowered and raised the long drill pipe (*foreground*) that the author and his team sent to the seafloor to extract rock cores from seamounts.**

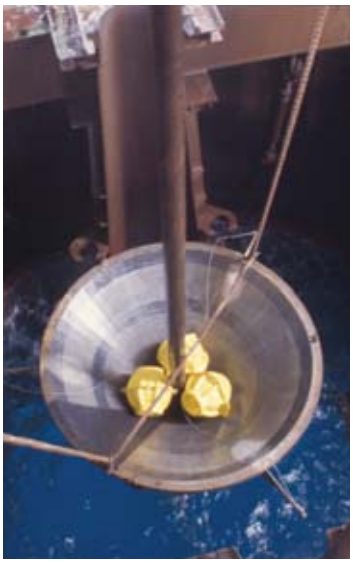
COURTESY OF JOHN A. TARDUNO (*drill*); KEVIN HAND (*illustration*)

[RESEARCH TOOL]

CLUES FROM ROCK MAGNETISM

Magnetic studies were key to revealing flaws in the old view of the Hawaiian-Emperor chain's evolution. When lava solidifies, certain minerals lock in the inclination, or angle, of the earth's magnetic field at that latitude (*white arrows in details*). The minerals line up parallel to the planet's surface at the equator (*bottom*), perpendicular to it at the magnetic poles, and at intermediate angles at mid-latitudes (*top*). Should a rock move, it will retain its original magnetic inclination. If the chain developed as a plate moved over a fixed hotspot, magnetic inclinations in seamount rocks would have matched those in rocks from Hawaii, but they did not.





▲ **CONE is being dispatched to the seafloor through an opening, called a moon pool, in the center of the *JOIDES Resolution.* Such cones helped to position the drill pipe that brought up rock cores for magnetic analysis.**

We compared our new result with a study done in 1980 by Masaru Kono, then at the Tokyo Institute of Technology, using ODP's predecessor, the Deep Sea Drilling Project. He had taken samples of the 61-million-year-old Suiko seamount of the Emperor chain and found that it had formed at 27 degrees north. These were startling results. If the Hawaiian hotspot, now located at a latitude of 19 degrees north, were fixed, the Detroit and Suiko seamounts would have formed at the same latitude. The three latitude values differed, suggesting that the Emperor seamounts marked the trace of a moving plume. Among our colleagues, though, the results met with a reception notable for its air of indifference. All our thousands of laboratory measurements condensed down to a mere two points on a graph. Skeptics required more before they would reconsider the textbook plate-motion explanation of the Hawaiian chain.

A Leg Up

In late 1997 Cottrell and I began thinking about a new ocean drilling expedition. We chose drilling sites with the help of David Scholl of Stanford University and also invited Bernhard Steinberger, who had been modeling mantle flow for his Ph.D. dissertation at Harvard University, to join the effort. We sailed off onboard the Ocean Drilling Program's *JOIDES Resolution* in the summer of 2001 on a two-month expedition—called Leg 197—that took us to three of the Emperor seamounts: Detroit, Nintoku and Koko.

Before drilling, we conducted short seismic surveys to ensure we would recover flat-lying lava layers, eliminating one source of potential error. Once we got the samples on deck, a cadre of experts helped us analyze them, including Robert Duncan of Oregon State University, Thorvaldur Thordarson, then at the University of Hawaii at Manoa, Frederick Frey of M.I.T. and Clive Neal of the University of Notre Dame. To estimate the rock's ages, we examined microfossils in sediments lying on top of or intermixed with the lavas. The ship had a magnetism lab where we gauged the rock's magnetization. It would take many months of follow-up work in shore-based laboratories, including critical isotope geochronological work, to confirm our findings. But the overall picture was apparent by the time we returned to port in Yokohama.

The hotspot had clearly moved rapidly south. Its inferred velocity during the period from 81 million to 47 million years ago was more than four centimeters a year, comparable to that of tectonic plates. Corroborating this finding, we found no coral debris at the Detroit or Nintoku seamounts and only a smattering at the Koko seamount. If these islands had formed at Hawaii's tropical latitude, we would have expected coral reefs to have taken shape around them.

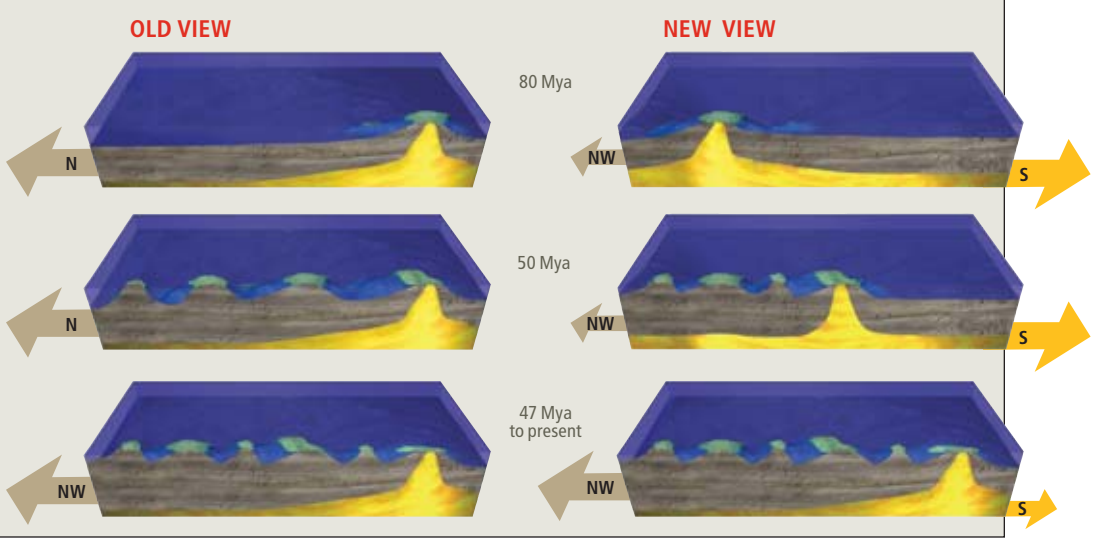
The implications are now rippling through the earth sciences, answering old questions and raising new ones. For example, one other geologic indicator of latitude is the type of sediments deposited in the deep oceans. Near the equator, sediments are rich in the calcium carbonate shells of plankton, which accumulate because of the high biological productivity of this region. Outside the equatorial zone, the sediments are carbonate-

COURTESY OF JOHN A. TARDUNO (*cone*); KEVIN HAND (*illustration*)

[CASE STUDY REVISITED]

WHAT REALLY HAPPENED

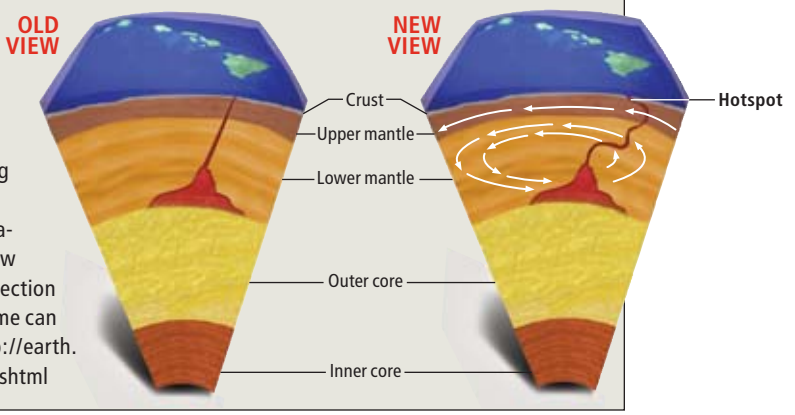
The magnetic work showed that the seamounts arose at progressively lower latitudes, with Detroit forming at about 36 degrees north and Koko at about 22 degrees north. So, although the old view of the Hawaiian-Emperor chain's evolution held that the hotspot stood still while the Pacific plate crossed over it (*left*), it is now clear that the hotspot migrated, too (*right*), heading south. (Arrow sizes represent relative speed.)



[NEW UNDERSTANDING]

BLOWING IN THE (MANTLE) WIND

Discovery that hotspots can travel has revised understanding of what they are. They are still defined as the tip-tops of mantle plumes that originate near the boundary between the earth's liquid core and the overlying viscous mantle. In the old view (*left*), though, the plumes remained fixed relative to the deep interior. In the new view (*right*), the plumes are swayed by convection within the mantle. The base of the plume can also move, as shown in a movie at http://earth.uni-muenster.de/dyn/plumedynamics.shtml



KEVIN HAND

poor. Sediments in cores from the Pacific Ocean up to 50 million years old do not fit the carbonate-rich pattern that one would expect if hotspots were fixed. Josep M. Pares and Ted C. Moore of the University of Michigan at Ann Arbor recently found that this paradox would be resolved if the Hawaiian hotspot was drifting southward.

Geologists may need to rewrite their textbooks about North America, too. Experts have known for a long time that large tracts of the American West did not form where they are now. These landmasses were pushed into their present positions by the long-gone plates that once composed the Pacific Ocean basin. Interactions between oceanic and continental plates are also responsible for the formation of major geologic features such as the Rocky Mountains. But the plate interactions have been estimated assuming that Hawaii's hotspot was a fixed reference point. Because it is not, geologists must revisit how western North America was built.

Pole Position

On a still larger scale, hotspot motion affects how researchers think about polar wander—rotation of the entire solid earth relative to the planet's spin axis. Polar wander is a confusing term in geophysics, because the phrase implies that the pole itself moves around. In fact, both the spin and magnetic axes remain almost fixed in absolute space; it is the land and seafloor that wander. The sinking of tectonic plates might shift the earth's mass distribution and cause an imbalance of forces, like a washing machine with a lopsided load of clothes. To rebalance itself, the entire planet would rotate. In the extreme case, Florida might wind up at the North Pole or Greenland might become a tropical island. This process differs from plate tectonics because the relative positions of the plates would remain the same.

In the 1980s geologists used the assumption of hotspot fixity to reconstruct plate motions and pinpoint the past locations of the earth with respect to its spin axis. The data suggested the earth had migrated up to 20 degrees relative to the axis over the past 130 million years. Our findings refute that claim: the hotspots moved, not the entire earth. So hotspots can be a false beacon for plate motions and polar wander.

The deepest implication of hotspot mobility relates to the earth's mantle. The hotspot may still be rooted in the deep mantle, but its base may move around, and the rising plume may be bent by the mantle flow. More radically, the concept of plumes itself has come under scrutiny. Don Anderson of Caltech has argued that hotspot plumes may not, in fact, be rooted in the lower mantle. They may instead be shallow phenomena, emerging from the upper layers of the mantle or lower layers of the crust. Others think plumes come in all shapes and sizes and originate at various layers within the planet.

As dramatic as our discoveries on hotspot mobility have been, they do not mean that all of present geologic understanding must be overturned. Science seldom works like that. The remarkable age progression and the sheer volume of magma marked by the Hawaiian-Emperor chain show that the Hawaiian hotspot is still closest to the ideal envisioned by Wilson and Morgan. But rather than being fixed in the deep mantle, it has had an unexpected mobility. A simple picture has given way to a complicated one. Both plates and hotspots move, and the observed effects can reflect a combination of both—challenging scientists to determine the contribution of each. Underappreciated until now, turmoil in the mantle deserves new respect. ■

MORE TO EXPLORE

Fixed Hotspots Gone with the Wind. Ulrich Christensen in *Nature,* Vol. 391, pages 739–740; February 26, 1998.

The Emperor Seamounts: Southward Motion of the Hawaiian Hotspot Plume in Earth's Mantle. John Tarduno et al. in *Science,* Vol. 301, pages 1064–1069; August 22, 2003.

Geophysics—Hotspots Come Unstuck. Joann Stock in *Science, ibid.,* pages 1059–1060.

Animations of plate tectonics processes are available in the Chapter 8 section at the Web site "Exploring Earth Visualizations": **www.classzone.com/books/earth_science/terc/navigation/visualization.cfm**

Tarduno's University of Rochester Paleomagnetic Research Group Web site is at **www.earth.rochester.edu/pmag**, and more information on the Integrated Ocean Drilling Program is at **www.iodp.org**

The Human Instrument

When judged by its size, our vocal system fails to impress as a musical instrument. How then can singers produce all those remarkable sounds? By Ingo R. Titze

KEY CONCEPTS

- Although the human vocal system is small, it manages to create sounds as varied and beautiful as those produced by a variety of musical instruments.
- All instruments have a sound source, a resonator that reinforces the basic sound and a radiator that transmits the sound to listeners.
- A human's sound source is the vibrating vocal folds of the larynx; the resonator is the sound-boosting airway above the larynx; and the radiator is the opening at the mouth.
- The human voice can create such an impressive array of sounds because it relies on nonlinear effects, in which small inputs yield surprisingly large outputs.

—The Editors

The human vocal system would not receive much acclaim if instrument makers placed it in a lineup of traditional orchestral instruments. Arranged by size, for example, the voice box (larynx)—and the airway it sits in—would be grouped with the piccolo, among the smallest of mechanical music makers. And yet experienced singers compete well with all man-made instruments, one on one and even paired with full orchestras. Recent investigations of how our singing voice generates a remarkable range of sounds have revealed surprising complexity in the behavior of the vocal system's elements and in the ways they interact.

For more than half a century, scientists explained the voice's ability to create song by invoking a so-called linear theory of speech acoustics, whereby the source of sound and the resonator of sound (or amplifier) work independently [see "The Acoustics of the Singing Voice," by Johan Sundberg; Scientific American, March 1977]. Researchers have now learned, however, that nonlinear interactions—those in which source and resonator feed off each other—play an unexpectedly crucial role in generating human sound. Such insights now make it possible to describe how great singers produce those amazing sounds.

Music-Making Keys

Structural and operational shortcomings in the human vocal apparatus are apparent in all its parts. To make music, an instrument needs three basic components: a sound source that vibrates in the air to generate a frequency that we perceive as pitch, together with higher frequencies that define the timbre (sound color); one or more resonators that reinforce the fundamental frequency by increasing its vibration strength; and a radiating surface or orifice that transfers the sounds to free air space and, eventually, to a listener's ear.

In the case of, say, a trumpet, a player's lips vibrate as lung-pumped air rushes between them into a cup-shaped mouthpiece to create a fundamental frequency and several higher frequencies that are called overtones. The instrument's metal tubes serve as the resonators, and the expanding aperture of the horn radiates the sound. Trumpeters alter fundamental frequency by modifying the lip tension and by pressing the valves to change the effective length of the tubes. Or take a violin: the strings vibrate to create

AARON GOODMAN

AMAZINGLY FLEXIBLE, the human voice creates sounds as rich and complex as those of conventional musical instruments—but with much smaller equipment.

pitches, the central air cavity and wooden top supply resonance, and the *f* holes in the top plate help to send the sound into the surrounding air.

A singer, on the other hand, relies on vibrating vocal folds, blowing air across them to generate the sound frequencies. Vocal folds are two small bundles of specialized tissue, sometimes called "vocal cords," that protrude pouchlike from the walls of the larynx. They generate a fundamental frequency by rapidly oscillating as they contact each other, separate and come in contact again. The glottis (the space between the folds) opens and closes. The laryngeal vestibule, an airway passage just above the larynx, acts like the mouthpiece of the trumpet to couple the sound to the remaining part of the resonator known as the vocal tract. The lips radiate the sound outward like the bell of the trumpet.

Instrument manufacturers examining the vocal folds, which are collectively the size of your thumbnail, would not find their potential for making orchestral musical sounds impressive. Beyond their small size, one immediate objection would be that they would seem too soft and spongy to sustain vibration and create a variety of pitches.

Nature, biology's instrument maker, might respond that although the folds are certainly undersized, the airways can produce enough resonance to reinforce the sound of the larynx substantially. But here, too, the musical instrument maker would probably still fail to be persuaded: the typical air tube extends just 15 to 20 centimeters above the larynx and 12 to 15 centimeters below it, no more than the length of a piccolo. The rest of the body contributes little or nothing. Wind instruments that approximate the pitches created by the human voice (trombones, trumpets, bassoons) typically contain much longer tubes; the bell and valves of a trumpet, for instance, uncoil to about two meters and those of a trombone to about three meters.

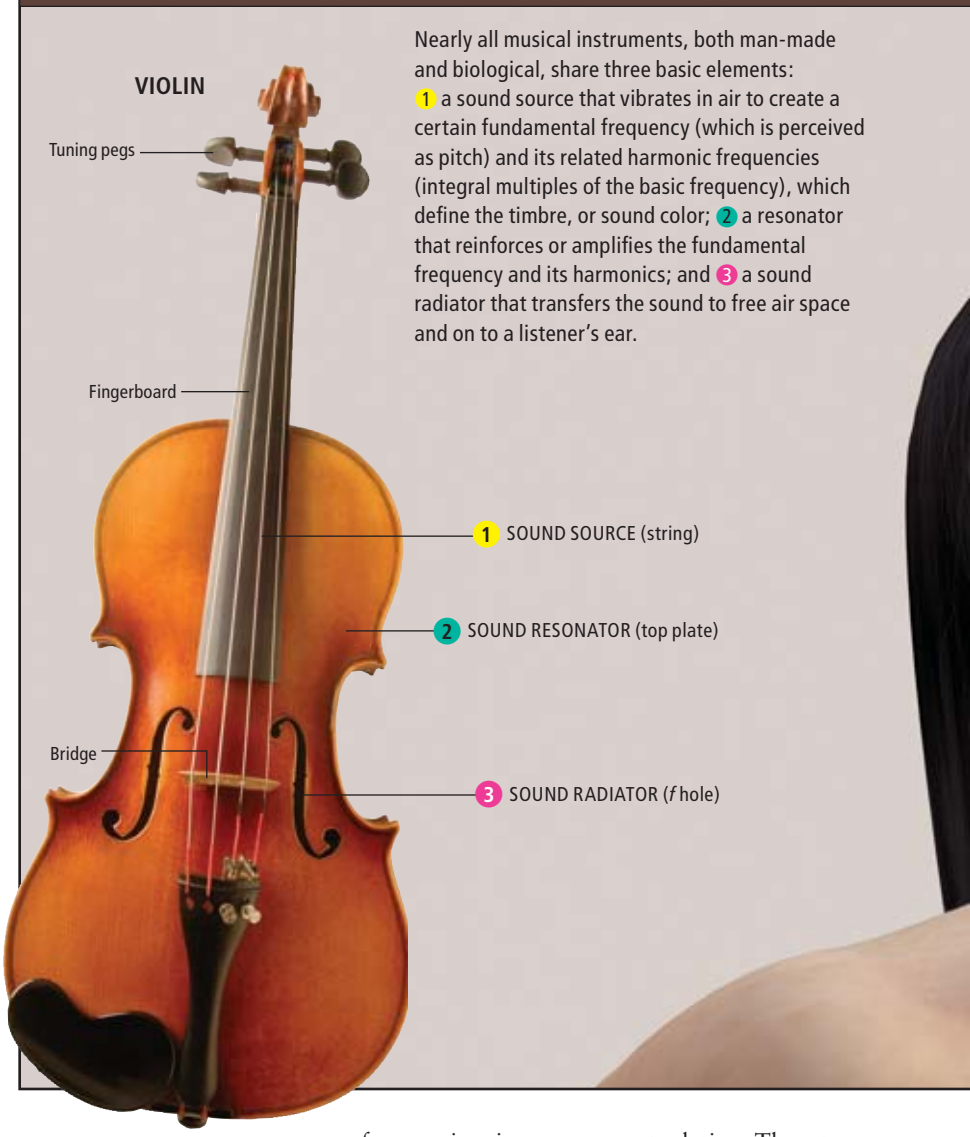
Source Design

To understand how nature the instrument maker has developed the vocal folds that perform beyond expectations, first consider some standard requirements for sound sources. For a reed or string to sustain its vibration, it needs to be made of an appropriately elastic material so it can snap back when deformed. Elasticity is measured by its stiffness (or, conversely, flexibility) or its tension: a reed has a bending stiffness; a string vibrates under tension. Generally, a sound source's stiffness or tension determines the sound frequencies via a square root relation. Thus, to make a steel string of a given length double its frequency (raise the pitch by an octave), one must quadruple the string tension. This rather stringent requirement may limit the range of frequencies that can reasonably be obtained by altering a source's stiffness or tension.

Fortunately, a player can also change the frequency of a sound source's vibration by effectively lengthening or shrinking the oscillating element. Within a vibrating string, for instance, frequencies are inversely proportional to the length of the vibrating segment. By pinning the string on one end with the finger, a player selects different frequencies. If a string's vibrating length is cut in half without changing the tension, for example, the vibration frequency doubles. To produce a wider range of frequencies, a single

[THE BASICS]

HOW INSTRUMENTS MAKE MUSIC

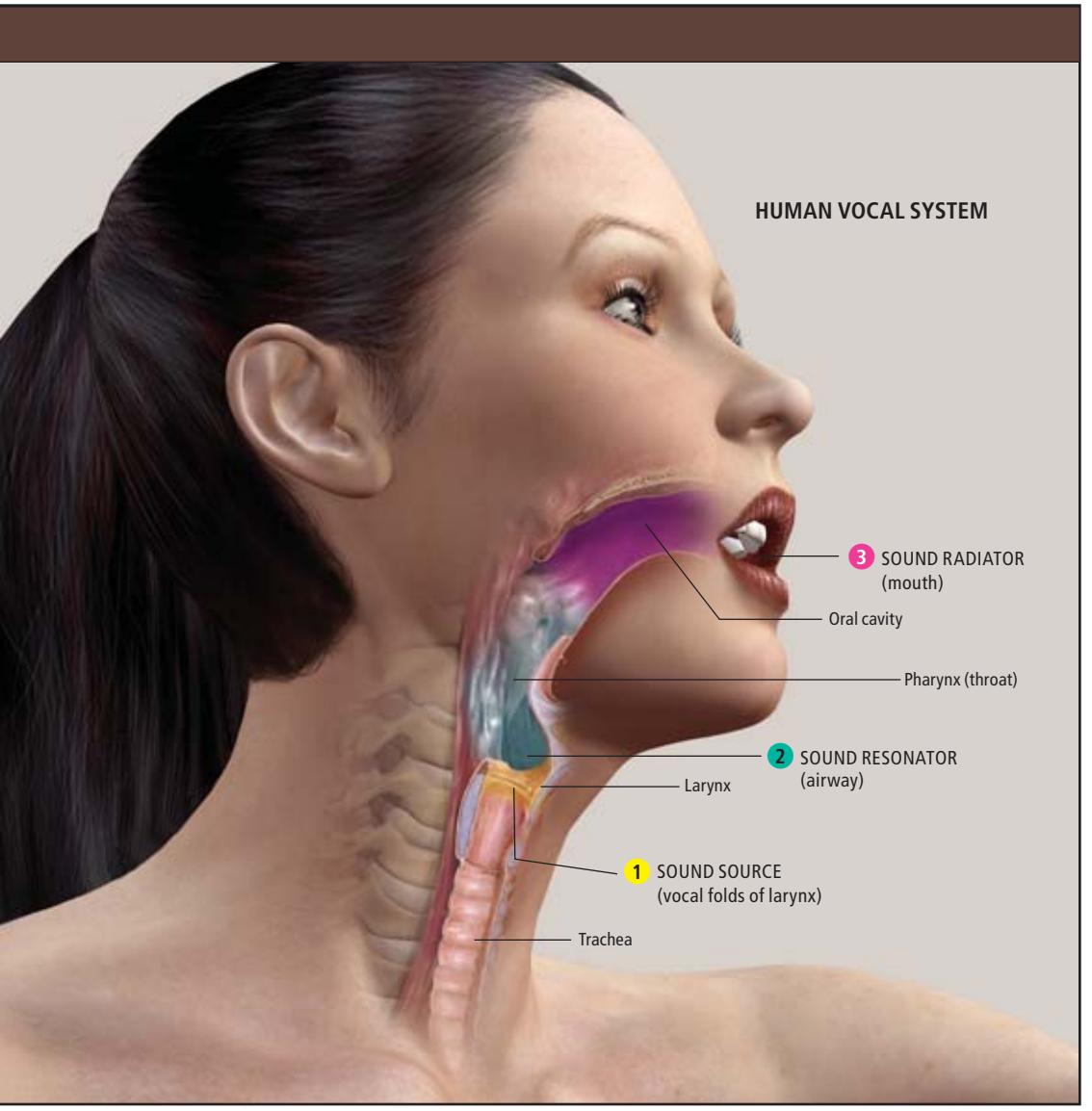


Nearly all musical instruments, both man-made and biological, share three basic elements: 1 a sound source that vibrates in air to create a certain fundamental frequency (which is perceived as pitch) and its related harmonic frequencies (integral multiples of the basic frequency), which define the timbre, or sound color; 2 a resonator that reinforces or amplifies the fundamental frequency and its harmonics; and 3 a sound radiator that transfers the sound to free air space and on to a listener's ear.

LINEAR VS. NONLINEAR

Voice scientists used to explain the performance of the human vocal system in terms of linear effects, ones in which the outputs of a function are proportional to the inputs (and so can be represented as a line, for example). More recently, researchers have concluded that the human vocal system behaves nonlinearly. In a nonlinear feedback system, small changes can result in disproportionately large effects.

STEVE DIBBLEE/*iStock Photo*



musical instrument often uses multiple strings.

String instruments, then, have three distinct mechanisms for changing frequency: altering the length of a string, modifying its tension, or skipping to another string. Players of stringed instruments typically set the tensions by turning pegs around which the strings are wrapped; the strings retain this same tension between end points. Players almost never can manipulate both the length and tension simultaneously.

The Little Source That Could

In playing the human vocal folds, in contrast, singers must do what no other string instrument can do: vary the length and tension of the vibrating material simultaneously to change frequency. Rather than pinning down a vocal fold with a finger to shorten its effective length, we use muscles to shift its end points. But should we lengthen or shorten the vocal folds to raise frequency? An argument could be made for either adjustment. Longer vocal folds would vibrate at lower frequency, but tenser folds would vibrate at higher frequency.

The physics formula describing the frequency of a string fixed at both ends under tension says that to get the maximum increase in frequency, one should increase the tension (actually the tensile stress, or tension per cross-sectional area) while decreasing the length. Such a response requires an unusual material, because most materials can increase tension (stress) only when they are elongated. Think of a rubber band; pull on it, and it tightens up. Thus, length and tension are in competition for changing frequency.

[THE AUTHOR]

Ingo R. Titze, a world leader in the scientific study of the human voice, has published more than 500 articles on the topic. He currently serves as the University of Iowa Foundation Distinguished Professor in that institution's department of speech pathology and audiology, and he directs the National Center for Voice and Speech (www.ncvs.org) at the Denver Center for the Performing Arts. Titze, who received his Ph.D. in physics from Brigham Young University in 1972, teaches singing and sings in multiple styles, including opera, Broadway and pop.

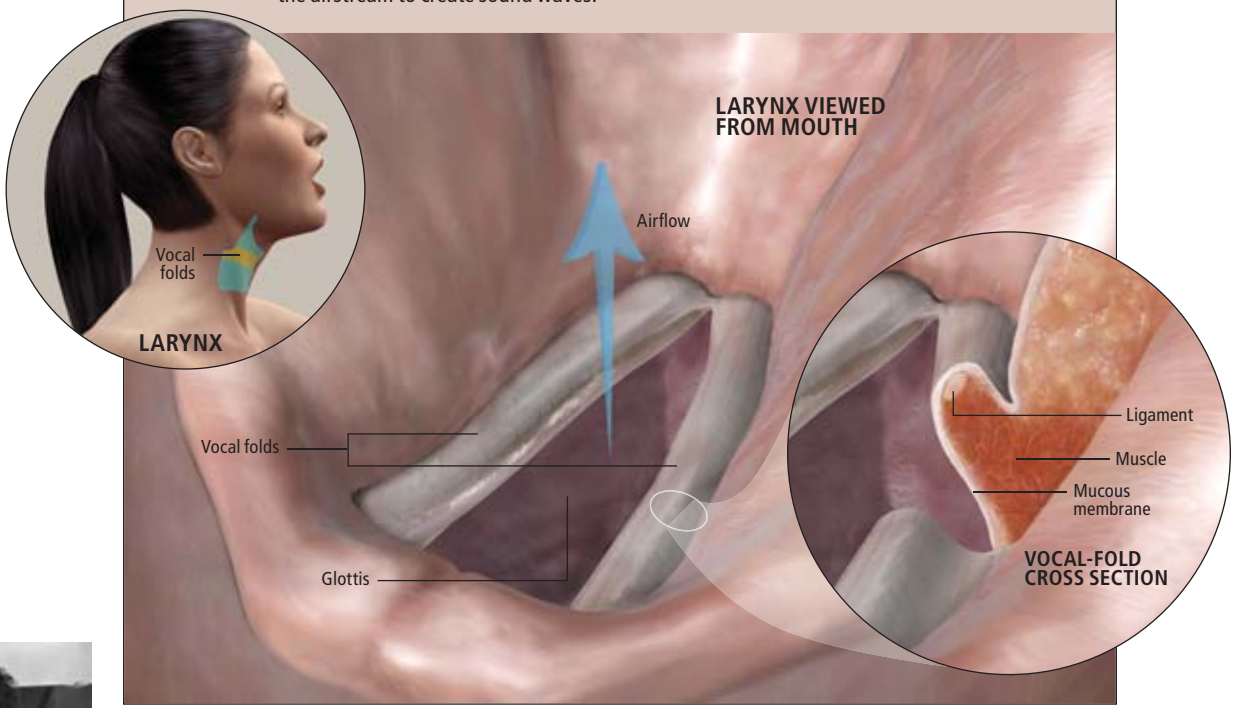
SHRIEK ROCKER Steven Tyler is celebrated for his ability to scream tunefully. Aerosmith's lead singer creates that extreme sound by using a large amount of nonlinear effects in his vocalizations.

COURTESY OF INGO R. TITZE (*Titze*); GEORGE PIMENTEL *Wirelmage/Getty Images (Tyler)*; ADAM QUESTELL (*illustration*)

[HUMAN SOUND SOURCE]

HOW OUR VOCAL FOLDS WORK

Unlike violin strings, the human sound source—the vocal folds (or vocal cords) in the larynx—has a complex, three-part structure that allows us to generate several octaves of frequencies. At the core of each fold is a stringlike ligament (*cross section*). Internal to the ligament are contractile muscles. And covering it all is a highly flexible mucous membrane. Each component brings a special capability to the whole. The ligament's tensile stress rises rapidly with elongation (by muscles that move the cartilages attached to the folds), which helps to produce higher frequencies. The vocal-fold muscle can increase tensile stress as it contracts. In doing so, it generates an even larger frequency range. The soft, pliable surface of the outer membrane, which oscillates like a flag in the wind as air from the lungs passes over it, exchanges vibrational energy with the airstream to create sound waves.



BROADWAY STAR Ethel Merman belted out songs with precise enunciation and pitch so the audience could hear her even without amplification. The female "belt" voice gains resonance from vocal-tract inertive reactance [*see box on opposite page*], which boosts the second harmonic frequency (double the fundamental).

Nature has addressed these problems by constructing the vocal folds out of a three-part material that displays properties not found in standard instrument strings. One component is a ligament that looks somewhat stringlike, which is why the folds came to be called "cords" popularly. Scientists have shown in biomechanical tests that the stress in this ligament rises nonlinearly when it is stretched just a little; it can be virtually limp when short but impressively tense when elongated. Stretching its length from 1.0 to just 1.6 centimeters, for example, can raise its internal stress by a factor of 30, which would yield a frequency change ratio of more than 5 to 1 (recall the square root relation mentioned earlier). But the fact that the length increases by 60 percent lowers the vibration rate, bringing the true frequency ratio back to around 3 to 1, about one and a half octaves in musical terms. Most of us speak and sing in this frequency range, but some singers can produce as much as four to five octaves, which is still considered extraordinary by scientists.

Complex Cords

Biology has also found a second way to expand the pitch range of the vocal folds, including a material that can increase in tension as it *shortens,* namely, muscle tissue. The internal contraction of muscle fibers can raise the stress between a vocal fold's end points, even when the fold itself shortens. About 90 percent of the volume of the vocal fold is muscle tissue. In essence, nature has solved the pitch problem largely by growing a group of strings side by side as a laminate, with some layers having contractile properties and others not. But how can this complex tissue be kept in vibration when it cannot be bowed or repeatedly plucked inside the larynx? The only source of energy available to deform the folds and thereby induce vibration—the way that wind passing across a flag makes it flap—is air flowing from the lungs. A muscle and a ligament alone would be too stiff to develop such vibrations as air passes over their surfaces. For the needed air-driven oscil-

BETTMANN/CORBIS (*Merman*); ADAM QUESTELL (*illustration*)

lation to occur, a soft, pliable surface tissue is required, one that can respond to the airstream by generating waves akin to those the wind forms at the surface of the ocean [see "The Human Voice," by Robert T. Sataloff; Scientific American, December 1992].

And indeed, the folds have a third layer, a mucous membrane that stretches over the muscle-ligament combination to provide this energy-transfer function. This mucosa, which consists of a very thin skin (epithelium) with a fluidlike substance underneath, is easily deformed and can support a so-called surface wave. My colleagues and I have shown mathematically that this airstream-driven wave sustains vibration. The buckling, ribbonlike motion often makes the tissue look like it is folding bottom to top, which is how the name "vocal fold" arose.

Playing the Vocal Folds

How can this triple-decker system be played over several octaves so as to produce a single frequency? Only with much experience and dexterity. Chaotic effects always lurk in the background during vocalizations as multiple natural (freely vibrating) frequencies compete in these tissues for dominance. This competition may result in unexpected pitch jumps or roughness in the sound [see "The Throat Singers of Tuva," by Levin Edgerton; Scientific American, September 1999].

For low pitches and moderate-to-loud sound volumes, the singer activates the vocal fold muscle and sets all the layers into vibration. The vocal folds are short, and the muscle stress largely determines the pitch. In this case, the mucosa and the ligament are both relaxed and serve mainly to propagate the desired surface waves for self-sustained oscillation. For the sound volume to be reduced at these pitches, the muscle does not vibrate and is used only to adjust the vocal-fold length. It is the combined elasticity of the mucosa and ligament that determines the frequency. To create high pitches, the singer elongates the vocal fold; ligament stress alone then dictates the frequency while the mucosa carries the surface wave.

It is not hard to imagine the complicated control system and innervation of the laryngeal muscles needed to finely regulate these tensions

DID YOU KNOW?

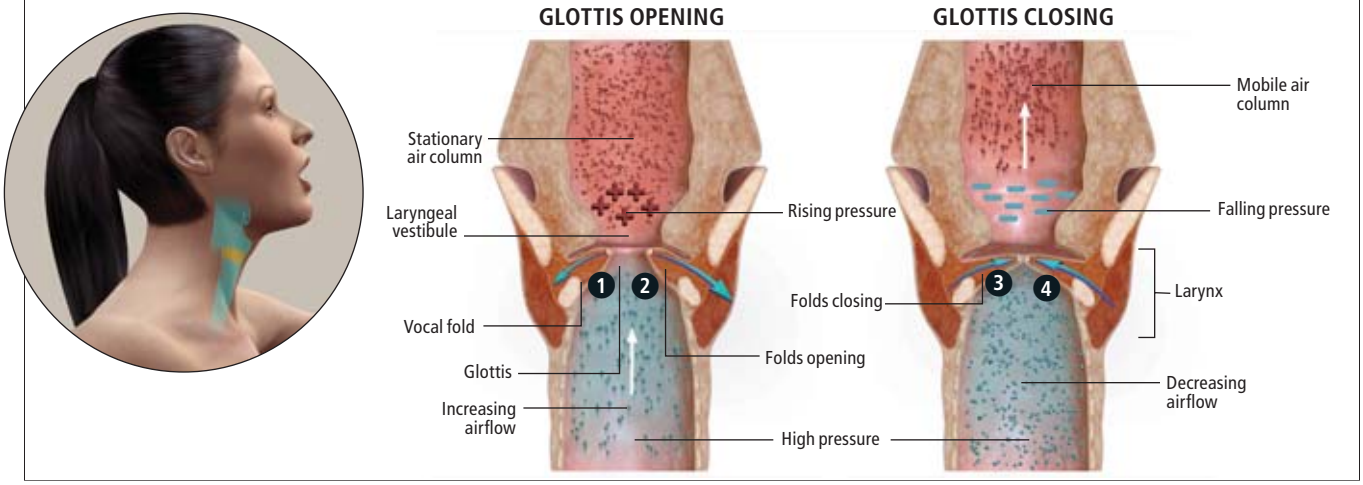
Humans tend to think of the entire body as the human instrument, which would make it comparable in size to a double bass. But most of the human body contributes nothing to the sound—neither the chest, the back, the belly, the buttocks nor the legs. All the sound comes from the voice box (larynx) and the air passages.

[HUMAN SOUND RESONATOR]

HOW THE VOCAL AIRWAYS AMPLIFY SOUND

Singers use a nonlinear energy-feedback process in the laryngeal vestibule (the airway above the larynx) to resonate, or amplify, sounds created by the vocal folds. This process, called inertive reactance, occurs when singers create special conditions in the vestibule to provide an extra, precisely timed "kick" to each cyclic opening and closing of the folds that reinforces their vibration to create stronger sound waves.

The kick comes in when the motion of the air column in the vestibule lags with respect to the movement of the vocal folds. When the vocal folds start to separate at the beginning of an oscillation (*1*), lung-driven air flows into the glottal space between the folds and presses against the motionless air column in the vestibule. The inertia of the stationary air column raises the air pressure in the glottis, which drives the folds even farther apart (*2*). Then the lungs begin to accelerate the air mass upward. As the air column moves, the elastic recoil of the folds begins to send them back together to close the glottis, cutting off the airflow from the lungs (*3*). Those responses leave a partial vacuum in the glottis that acts to slam the folds together strongly (*4*). Thus, like a well-timed push on a kid's swing, the inertive reactance—the push-pull action—of the air in the laryngeal vestibule augments each swing of the vocal folds, creating resonance.

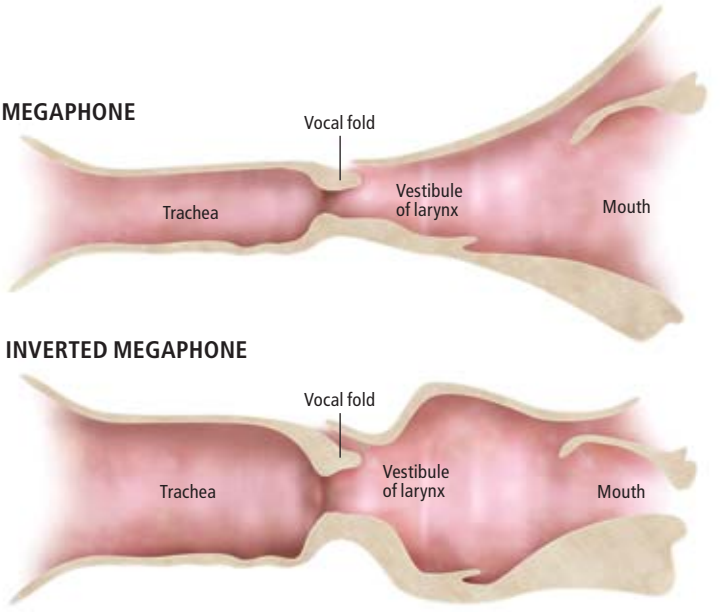


ADAM QUESTELL

[HUMAN SOUND RADIATOR]

BIG MOUTHS AND SMALL MOUTHS

Acting as a tube resonator, the vocal tract adopts certain shapes to better project certain pitches and resonant overtones. To produce powerful high notes, belters often open their mouths as wide as possible. This so-called megaphone configuration resembles a trumpet (*top*), with the vocal folds and vestibule serving as the "lips and mouthpiece" and the mouth as the "horn." Other singing styles are better produced when the vocal tract takes on an inverted megaphone shape—that is, with the mouth narrowed (*bottom*).



DAME Joan Sutherland knew instinctively that some vowels cannot be used when singing certain pitches. The Australian soprano changed some of the vowels in her opera lyrics (even to the point of mispronouncing the words) to best match them with the desired pitches.

to produce a desired frequency and volume level. Laryngeal muscles outside the vocal folds precisely coordinate length changes in the vocal fold. During these complicated manipulations, voice quality may suddenly change, a phenomenon known as registration. It is caused to a large extent by overusing or underusing the vocal-fold muscle to regulate tension. Singers use registration artistically to present two contrasting sounds to the listener, as in yodeling. If a singer involuntarily or accidentally changes register, however, it can cause embarrassment, because such a slip suggests a lack of control of the singer's instrument.

Resonating Airways

In musical instruments, the resonator for the most part determines the instrument size, but singers have to make do with a pint-size resonator. The human resonator, however, performs effectively despite its overt limitations.

In a musical instrument, boards, plates, kettles, horns or tubes typically act to reinforce and amplify the frequencies that the sound source produces. In the violin, for instance, the strings pass over a bridge support that connects to the top plate, which has been carefully fashioned to vibrate sympathetically at many of the same natural frequencies that the strings can produce, thereby boosting them. The air mass between the top and bottom plates can also oscillate at the strings' natural frequencies. In many brass and woodwind instruments, the horn (with its valves) is designed to match many of the source frequencies at whatever pitch is played.

Because physical law dictates that all steady (continuous) sounds are composed of source frequencies that are harmonically spaced—meaning that all source frequencies are integer multiples (2:1, 3:1, 4:1, …) of the fundamental—the resonator must often be quite large to accommodate these wide frequency spacings. This physical law dictates that trumpet horns are 1.2 to two meters long, trombone horns stretch three to nine meters, and French horn tubing uncoils from 3.7 to 5.2 meters.

Nature is stingy with the size of the singer's resonator. The total size of the human airway above the vocal folds is only about 17 centimeters long. The lowest frequency that can be resonated is around 500 hertz (cycles per second)—and half that when certain vowels are sung, such as /u/ or /i/ (as in "pool" or "feel"). Because the vocal tract is a resonant tube that is nearly closed at one end, its resonant frequencies include only the odd-integer multiples (1, 3, 5, …) of the lowest resonance frequency. Therefore, this short tube can resonate simultaneously only the odd harmonics of a 500-Hz source frequency (500 Hz, 1,500 Hz, 3,500 Hz, …). And because the vocal tract cannot change tube length with valves or slides (other than a few centimeters by protruding a lip or lowering the

IRA NOWINSKI *Corbis (Sutherland)*; ADAM QUESTELL *(illustration)*

larynx), our resonator seems as if it should be hopelessly restricted in what it can do.

Resonating a Short Tube

Here again recent studies indicate that nonlinear effects come to the rescue. This time it is a nonlinear interaction among the system's elements. Rather than reinforcing each harmonic with a specific tube resonance (as occurs, for example, in organ pipes of different sizes, each of which resonates certain harmonics), our short vocal tract reinforces a cluster of harmonics simultaneously by using an energy-feedback process. The vocal tract can store acoustic energy in one part of the vibration cycle and feed it back to the source at another, more advantageous time. In effect, the vocal tract gives a "kick" to each cycle of oscillation of the vocal folds so as to increase the amplitude of vibratory motions. In analogy to pushing someone on a playground swing, this cyclic kick resembles a carefully timed push to boost the amplitude (travel distance) of the swing's oscillations.

The ideal timing of the kick comes when the movement of the air column in the tube is delayed with respect to the movement of the vocal folds. Scientists say that the air column then has inertive reactance (slow or sluggish response to an applied pressure). Inertive reactance helps to sustain the flow-induced oscillation of the vocal folds in a profound way [*see box on page 99*].

When the vocal folds begin moving apart at the inception of a vibratory cycle, air from the lungs starts to flow into the glottal space between them and begins pushing on the stationary air column located just above in the laryngeal vestibule. Air pressure in and above the glottis rises as the air column accelerates upward to allow new air to fill in behind it. This pressure increase pushes the folds even farther apart. When elastic recoil springs the folds back from the walls to close the glottis, the flow of air through the glottis subsides. Because of inertia, though, the air column continues to move up, leaving a partial vacuum in and above the glottis that acts to slam the folds more strongly together. Thus, like a well-timed push on a kid's swing, the inertive reactance of the air in the vocal tract augments each swing of the vocal folds with a push-pull action.

Still, the vocal tract does not automatically behave in this inertive way for all vocal shapes. A singer's task is to adjust the shape of the vocal tract (by carefully selecting favorable "singing" vowels) so that inertive reactance is experienced over most of the pitch range—no easy task.

ETHAN MILLER *Corbis*

ITALIAN TENOR Luciano Pavarotti, famed for the brilliance and beauty of his tone, produced the rich resonance in his voice by fine-tuning nonlinear inertive reactance in his throat.

MORE TO EXPLORE

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Megaphone Mouth

Different singing styles rely on different vocal tract shapes to make optimal use of inertive reactance. In producing an /æ/ vowel (as in "mad"), the vocal tract approximates a megaphone shape. A small cross section at the glottis is paired with a large opening at the mouth [*see box on opposite page*]. Singers can find inertive reactance as high as 800 or 900 Hz for males and 20 percent higher for females. At least two harmonic source frequencies can achieve inertive reactance for fairly high pitches, and several more can for low pitches. This fact means that one strategy for obtaining powerful high notes is for the singer to open the mouth as wide as possible, as in belting or calling. When the vocal tract adopts this megaphone configuration, it approximates the shape of an amputated trumpet (with no coiling tube or valves, but with a bell, or horn).

An alternative approach to reinforcing vocal-fold vibration with inertive reactance is to adopt the so-called inverted-megaphone shape, in which the laryngeal vestibule, the "mouthpiece," is kept narrow, the pharynx (the part of the throat situated immediately behind the mouth and nasal cavity) is expanded as widely as possible and the mouth is narrowed somewhat. This configuration is approximated to verbalize the /u/ vowel (as in "took"). The inverted-megaphone technique is ideal for female classical singers who wish to sing in the middle of their pitch range and male classical singers who wish to sing in the high part of their pitch range. Classical training involves finding more regions of the singing range where the vocal tract provides inertive reactance for the source frequencies, at all pitches and for many different vowels. The training also involves getting a "ring" into the voice, which is accomplished by the combination of the narrow vestibule and the wide pharynx. Singing teachers use terms such as "covering" the voice or "turning it over" to describe the process of choosing just the right vowel for the given pitch so that most of the source frequencies experience inertive reactance.

Singing styles are based on what human biology can offer to produce an acoustically efficient instrument. Researchers who study the elements of the human vocal system, and the unexpected ways in which it functions, are garnering an ever greater understanding of how accomplished singers ply their art. Both scientists and singers will benefit substantially from continued close cooperation and study. ■

Cooking Up Bigger Brains

Our hominid ancestors could never have eaten enough raw food to support our large, calorie-hungry brains, Richard Wrangham claims. The secret to our evolution, he says, is cooking BY RACHAEL MOELLER GORMAN

Richard Wrangham has tasted chimp food, and he doesn't like it. "The typical fruit is very unpleasant," the Harvard University biological anthropologist says of the hard, strangely shaped fruits endemic to the chimp diet, some of which look like cherries, others like cocktail sausages. "Fibrous, quite bitter. Not a tremendous amount of sugar. Some make your stomach heave." After a few tastings in western Uganda, where he works part of the year on his 20-year-old project studying wild chimpanzees, Wrangham came to the conclusion that no human could survive long on such a diet. Besides the unpalatable taste, our weak jaws, tiny teeth and small guts would never be able to chomp and process enough calories from the fruits to support our large bodies.

Then, one cool fall evening in 1997, while gazing into his fireplace in Cambridge, Mass., and contemplating a completely different question—"What stimulated human evolution?"—he remembered the chimp food. "I realized what a ridiculously large difference cooking would make," Wrangham says. Cooking could have made the fibrous fruits, along with the tubers and tough, raw meat that chimps also eat, much more easily digestible, he thought—they could be consumed quickly and digested with less energy. This innovation could have enabled our chimplike ancestors' gut size to shrink over evolutionary time; the energy that would have gone to support a larger gut might have instead sparked the evolution of our bigger-brained, larger-bodied, humanlike forebears.

In the 10 years since coming on his theory, Wrangham has stacked up considerable evidence to support it, yet many archaeologists, paleontologists and anthropologists argue that he is just plain wrong. Wrangham is a chimp researcher, the skeptics point out, not a specialist in human evolution. He is out of his league. Furthermore, archaeological data does not support the use of controlled fire during the period Wrangham's theory requires it to.

Wrangham, who first encountered chimps as a student of Jane Goodall's in 1970, began his career looking at the way ecological pressures, especially food distribution, affect chimp society. He famously conducted research into chimp violence, leading to his 1996 book *Demonic Males*. But ever since staring into that fire 10 years ago, he has been plagued with thoughts of how humans evolved. "I tend to think about human evolution through the lens of chimps," he remarks. "What would it take to convert a chimpanzeelike ancestor into a human?" Fire to cook food, he reasoned, which led to bigger bodies and brains.

And that is exactly what he found in *Homo erectus*, our ancestor that first appeared 1.6 million to 1.9 million years ago. *H. erectus*'s brain was 50 percent larger than that of its predecessor, *H. habilis*, and it experienced the biggest drop in tooth size in human evolution. "There's no other time that satisfies expectations that we would have for changes in the body that would be accompanied by cooking," Wrangham says.

The problem with his idea: proof is slim that any human could control fire that far back. Other researchers believe cooking did not occur until perhaps only 500,000 years ago. Consistent signs of cooking came even later, when Neandertals were coping with an ice age. "They developed earth oven cookery," says C. Loring Brace, an anthropologist at the University of

KATHLEEN DOOHER

RICHARD WRANGHAM

FLAME ON: Argues that the practice of cooking food, beginning with *Homo erectus*, ultimately enabled the human brain to evolve to its current large size.

INTO THE FRYING PAN: His theory has many skeptics because only scattered signs of fire use by *H. erectus* exist. One example: a Chinese site where *H. erectus* may have spat hackberry seeds into early campfires (producing spectacular sparks).

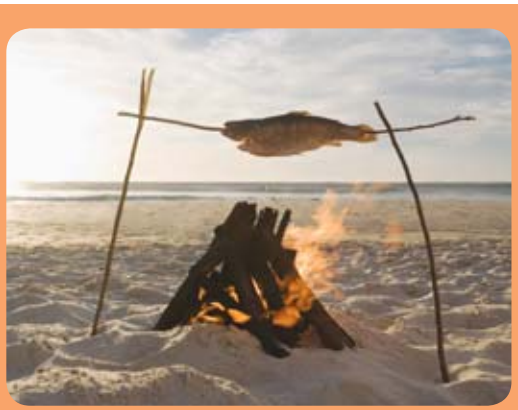
ON THE IMPORTANCE OF THE STOVE: "Everywhere, everyone expects a cooked meal every evening."

Michigan at Ann Arbor. "And that only goes back a couple hundred thousand years." He and others postulate that the introduction of energy-rich, softer animal products, not cooking, was what led to *H. erectus*'s bigger brain and smaller teeth.

So Wrangham did more research. He examined groups of modern hunter-gatherers all over the world and found that no human group currently eats all their food raw. Humans seem to be well adapted to eating cooked food: modern humans need a lot of high-quality calories (brain tissue requires 22 times the energy of skeletal muscle); tough, fibrous fruits and tubers cannot provide enough. Wrangham and his colleagues calculated that *H. erectus* (which was in *H. sapiens*'s size range) would have to eat roughly 12 pounds of raw plant food a day, or six pounds of raw plants plus raw meat, to get enough calories to survive. Studies on modern women show that those on a raw vegetarian diet often miss their menstrual periods because of lack of energy. Adding high-energy raw meat does not help much, either—Wrangham found data showing that even at chimps' chewing rate, which can deliver them 400 food calories per hour, *H. erectus* would have needed to chew raw meat for 5.7 to 6.2 hours a day to fulfill its daily energy needs. When it was not gathering food, it would literally be chewing that food for the rest of the day.

To prove that cooking actually does save energy, Wrangham partnered with Stephen Secor, a University of Alabama biologist who studies the evolutionary design of the digestive system. They found that the python—an animal model with easily studied gut responses—expends less effort breaking down cooked food than raw. Heat alters the physical structure of proteins and starches, thereby making enzymatic breakdown easier.

Wrangham's theory would fit together nicely if not for that pesky problem of controlled fire. Wrangham points to some data of early fires that may indicate that *H. erectus* did indeed tame fire. At Koobi Fora in Kenya, anthropologist Ralph Rowlett of the University of Missouri–Columbia has found evidence of scorched earth from 1.6 million years ago that contains a mixture of burned wood types, indicating purposely made fire and no signs of roots having burned underground (a tree struck by lightning would show only one wood type and burned roots). The discoveries are consistent with human-controlled fire. Rowlett plans next to study the starch granules found in the area to see if food could have been cooked there.



In contemplating the question of what stimulated human evolution, "I realized what a ridiculously large difference cooking would make," Richard Wrangham says.

C. LYTTLE *zefa/Corbis*

Still, most researchers state that unless evidence of controlled fire can be regularly confirmed at most *H. erectus* sites, they will remain skeptical of Wrangham's theory. Moreover, other food-based theories can explain the body and brain expansion without flames. One is the expensive tissue hypothesis, proposed in 1995 by Leslie C. Aiello, professor emeritus of biological

anthropology at University College London, and physiologist Peter Wheeler of Liverpool John Moores University in England. The main idea of the hypothesis—that smaller guts correlate with bigger brains in primates—fits with Wrangham's theory, but Aiello and Wheeler think that energy-dense animal-derived foods, such as soft bone marrow and brain matter, were the reason humans developed these characteristics, not cooking.

Lacking the proof for widespread fire use by *H. erectus*, Wrangham hopes that DNA data may one day help his cause. "It would be very interesting to compare the human and *Homo erectus* genetics data to see when certain characteristics arose, such as, When did humans evolve improved defenses against Maillard reaction products?" he says, referring to the chemical products of cooking certain foods that can lead to carcinogens.

Even without such evidence yet, some think Wrangham's theory is just the thing to shake up the field of human evolution. "It doesn't matter who develops these ideas," says Aiello, who is also president of the Wenner-Gren Foundation, which supports anthropological research. "You have to listen to what Richard is saying because he has some very interesting, original data. Sometimes the most creative ideas come from unexpected places." She points to Goodall, who surprised the world by proving that humans were not the only toolmakers. "It's one of the best illustrations I know of the value of primate research informing our knowledge of human evolution and adaptation," Aiello says.

If Wrangham's strange ideas turn out to be true, we can thank an early hominid Emeril Lagasse who picked a charred tuber out of a campfire and swallowed it. Without that person, we might never have been able to examine our origins—or enjoy a good grilled steak—in the first place. ■

Rachael Moeller Gorman is a writer based in Boston. A Q&A version of her interview with Wrangham is at **www.SciAm.com/ontheweb**

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Perpetual Reset Machine

By Mark Fischetti

A busy bowling alley might seem noisy, but behind the lanes the cacophony is significantly louder. As the heavy balls crash into the wooden pins, hefty motors, conveyor belts, pulleys and cams clatter behind each "pit," grabbing the wreckage from one collision while hoisting and arranging pins so they are ready for the next one.

For years pin boys stood at the lane ends, manually resetting pins and rolling the balls back to bowlers. Machines did not appear until 1946, when AMF Bowling, Inc., now in Richmond, Va., introduced the first "automated pinspotter." Brunswick Corporation in Lake Forest, Ill., later offered a competing "pinsetter," and the two companies still dominate the market today with technology that is strongly reminiscent of the original.

What has changed most are the bells and whistles designed to expand bowling's popularity. In the 1980s cameras were placed between the lanes, pointed at the pins, and wired to computers that automatically calculated bowlers' scores and displayed them overhead. More recently, a system of blacklights, fluorescent pins, laser beams, loud music and video screens has turned the ordinary routine into a dazzling late-night dance party promoted as cosmic, disco or "Xtreme" bowling.

A visit to the back end of a typical 24-lane alley, such as Cove Bowling Lanes in Great Barrington, Mass., reveals a mechanical engineer's paradise. Twenty-four steel, wood and rubber pinspotter machines relentlessly chunk along shoulder to shoulder; each one is about five feet tall, weighs about 2,000 pounds and collects, sorts and resets 10 pins in around eight seconds. Racks of spare belts, cams, rods, levers, oils and rags line the rear wall, looking like a cluttered auto repair garage. Cove Bowling Lanes head mechanic DJ Marks must inspect, clean and lubricate each machine every week. "It's pretty much a constant job," he says happily. "I do five machines a day—four on Fridays." He shows them off to enthusiastic patrons and says most proprietors will do the same. So on your next trip to the lanes, if you are not compiling a marvelous score, ask for a peek at the mechanical marvels instead.

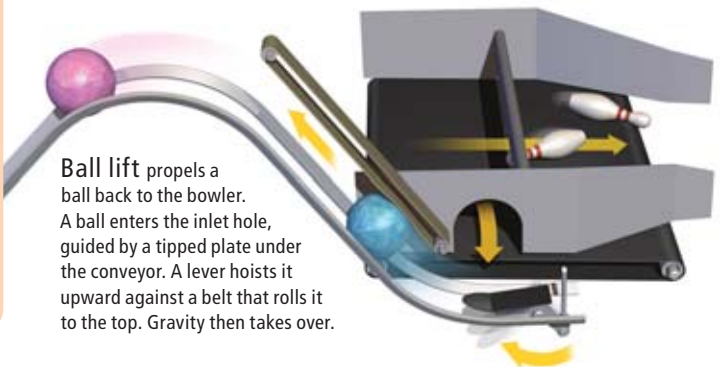
DID YOU KNOW...

HUMAN TARGET: Pin boys reset pins before machines came along. "You really had to work fast, or the bowlers would yell at you, 'Hey, get moving!'" recalls Paul Retseck, 84, who set pins in the 1930s for $1 a night in Michigan City, Ind. Drunken patrons sometimes tried to hurl balls at boys who were stooped over picking up pins: "We learned to hop up quick onto the side wall," Retseck says. *Above:* Subway Bowling Alleys in Brooklyn, N.Y., at 1 A.M., April 1910.

LOST BALL: Occasionally a ball does not return to the bowler. The most likely culprit is a pin that becomes lodged in the ball-return inlet hole, wedged under the return lever. An attendant must remove the pin, although a second bowled ball might knock it free, too.

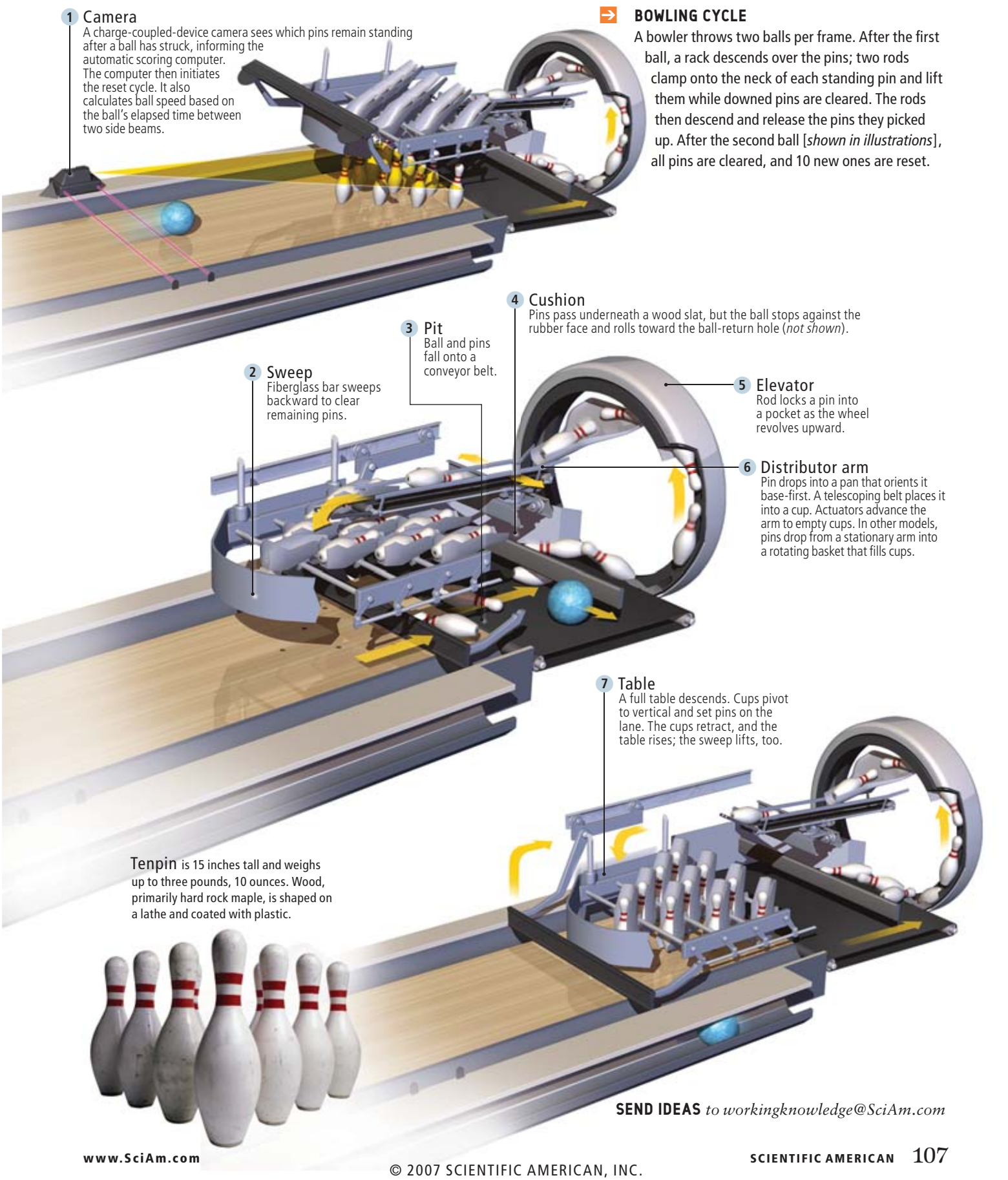
RESET: At times the sweep bar may stall on the lane. This usually occurs because the table did not receive all 10 pins. The missing pin prompts the arm to stay above the table instead of returning to its neutral position, which signals the sweep cycle to continue. A bowler can request help from an attendant by pressing the reset button.

Balls are most often made of resin. A core denser at the center (*shown*) creates a low radius of gyration; the ball rotates sideways more easily as it rolls forward and therefore hooks gently and steadily along the lane. Pushing core density outward creates a high radius of gyration; the ball rolls straight down the lane but then hooks sharply as its angular momentum builds.



Ball lift propels a ball back to the bowler. A ball enters the inlet hole, guided by a tipped plate under the conveyor. A lever hoists it upward against a belt that rolls it to the top. Gravity then takes over.

LIBRARY OF CONGRESS, PRINTS AND PHOTOGRAPHS DIVISION, NATIONAL CHILD LABOR COMMITTEE COLLECTION (*pinsetters*); C SQUARED STUDIOS *Getty Images (pins)*; GEORGE RETSECK (*illustrations*)



SEND IDEAS *to workingknowledge@SciAm.com*

Beasts with Soul ▪ Machines with Brains ▪ Bubble Baths with Meaning

BY MICHELLE PRESS

THE SOUL OF THE RHINO: A Nepali Adventure with Kings and Elephant Drivers, Billionaires and Bureaucrats, Shamans and Scientists, and the Indian Rhinoceros

by Hemanta Mishra. Lyons Press, 2008 ($24.95)

The subtitle may sound like hype, but it is a rare case of truth in labeling. Against the backdrop of political violence in Nepal—beginning with the massacre of the king's family in 2001 by the eldest son and ending with the Maoist insurgency this crisis spawned—Mishra tells the story of trying to save the greater one-horned Asian rhino from extinction. Kings did indeed play a pivotal role in the creature's conservation, and the murder of the recent king led to its now uncertain future. The exotic Tarpan ceremony, in which the Nepalese king must hunt and kill a male rhino and offer the beast's blood in a prayer for peace and prosperity, takes center stage. Mishra, a Nepalese wildlife biologist trained in the West, is not a professional writer, but his intelligence and wit make this a mesmerizing account that intertwines politics, conservation and tensions between the traditions of East and West.

THE DESIGN OF FUTURE THINGS

by Donald A. Norman. Basic Books, 2007 ($27.50)

A computer scientist who is the author of *The Design of Everyday Things* and many other articles and books on design and technology, Norman asserts that the intelligence of so-called smart systems is fundamentally limited: a machine cannot begin to know all the factors that go into human decision making. In fact, machines have become too smug, he says. From cars to refrigerators to scales, they misread our intentions. But of course, he argues, this doesn't mean we should reject their help. Instead we need to figure out a way to "socialize" them, to see that they recognize their limitations and improve their interactions with humans. Much of what he has to say will be familiar to those who have read his previous work, but if you are new to Norman, the book provides an enjoyable antidote to a lot of current hyperbole.

EXCERPT

EVOLUTION

Text by Jean-Baptiste de Panafieu. Photographs by Patrick Gries. Translated by Linda Asher. Seven Stories Press, 2007 ($65)

The Natural History Museum of Paris collaborated on these astonishing photographs from Gries to provide visual affirmation of evolution. Fleshing out the skeletal evidence are brief essays by de Panafieu and an even more succinct 250-year-old observation from the Comte de Buffon:

"Take the skeleton of a man. Tilt the pelvis, shorten the femur, legs, and arms, elongate the feet and hands, fuse the phalanges, elongate the jaws while shortening the frontal bone, and finally elongate the spine, and the skeleton will cease to represent the remains of a man and will be the skeleton of a horse." —*Buffon, 1753*

NEW AND NOTABLE BOOKS: HOLLYWOOD SCIENCE

1 **Don't Try This at Home: The Physics of Hollywood Movies**
by Adam Weiner. Kaplan Publishing, 2007 (paperbound, $17.95)

2 **Stereoscopic Cinema and the Origins of 3-D Film, 1838–1952**
by Ray Zone. University Press of Kentucky, 2007 ($42)

3 **Hollywood Science: Movies, Science, and the End of the World**
by Sidney Perkowitz. Columbia University Press, 2007 ($24.95)

4 **What's Science Ever Done for Us? What *The Simpsons* Can Teach Us about Physics, Robots, Life, and the Universe**
by Paul Halpern. John Wiley & Sons, 2007 (paperbound, $14.95)

5 **The Physics of *Star Trek***
by Lawrence M. Krauss. Revised and updated. Foreword by Stephen Hawking. Basic Books, 2007 (paperbound, $15)

EINSTEIN'S ENIGMA OR BLACK HOLES IN MY BUBBLE BATH

by C. V. Vishveshwara. Springer, 2006 ($27.50)

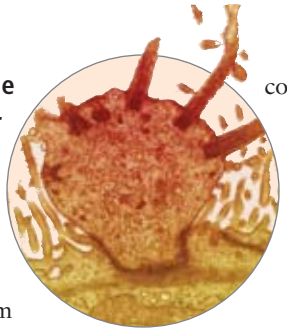
The author blends fiction, fantasy, physics and philosophy to tell the story of gravitation theory, focusing on Einstein's general relativity and the astrophysics of black holes. He not only succeeds at doing this; he entertains readers with delightful digressions and illustrates key concepts with wonderful cartoons, some purportedly scribbled on paper napkins. A theoretical physicist, Vishveshwara received his doctorate and taught in the U.S. before returning to his native India, where he has been a professor at the Raman Research Institute and the Indian Institute of Astrophysics.

How do we **remember smells** for so long if olfactory sensory neurons only survive for about 60 days?

—A. A. Bozorgi, Irvine, Calif.

Donald A. Wilson, a zoology professor at the University of Oklahoma and co-author of *Learning to Smell* (Johns Hopkins University Press, 2006), replies:

We recognize an old scent, despite having replaced at least a subset of the olfactory sensory neurons that first interacted with that odor, because the overall pattern of activity within the olfactory system remains relatively constant over time.



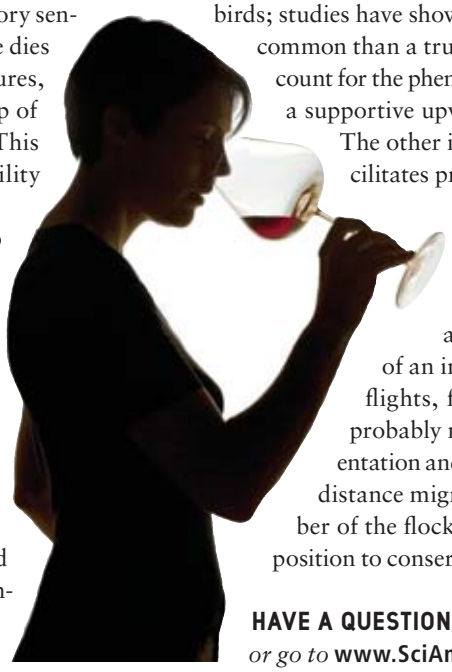
OLFACTORY neuron (*orange*)

Olfactory sensory neurons, which sit in the mucus in the back of the nose and relay data to the brain via axons (fingerlike projections that transmit information out from the cell body), are one of an increasingly large number of neuron types that are known to die and be replaced throughout life. Fortunately, they do not all die at the same time, and there are many thousands of olfactory sensory neurons that respond to any given scent.

The 2004 Nobel Prize in Physiology or Medicine went to Linda B. Buck and Richard Axel for their 1991 research showing that there is a huge family of genes that encode proteins called olfactory receptors. One of their important observations was that individual olfactory sensory neurons typically express just one of those genes. That is, signals from a given neuron provide information about odors that activate the specific receptor protein expressed by that cell. In fact, when an olfactory sensory neuron expressing a particular receptor gene dies and a new neuron expressing that same gene matures, the new neuron's axons plug into the same group of olfactory bulb neurons that its predecessor did. This phenomenon results in remarkable pattern stability over years, despite continual rewiring.

A single receptor protein, however, appears to bind (or recognize) many different odors. Thus, rather than having neurons that respond selectively to coffee or vanilla or Bordeaux, most individual cells respond (via their receptors) to submolecular features of the volatile chemicals coming from those objects. For example, an olfactory sensory receptor neuron may respond to a hydrocarbon chain of a particular length or to a specific functional group such as an alcohol or aldehyde.

Therefore, any given sensory neuron will respond to many different odors as long as they share a common feature. The brain (specifically, the olfactory bulb and the olfactory cortex) then looks at the combination of sensory neurons activated at any given time and interprets that pattern; the brain's interpretation is what you perceive as smell. With so many inputs contributing to the formation of a scent pattern, the absence of a small number of constituents does not appreciably change the pattern or the brain's perception.



Why do migratory birds fly in a **V formation**?

—J. F. Bowman, Corte Madera, Calif.

Bruce Batt, who retired in 2007 as chief biologist for Ducks Unlimited, a wetlands conservation group based in Memphis, Tenn., offers this explanation:

There are two well-supported and complementary explanations for why birds fly in formation. (Both V and J structures are typical and readily recognizable flight formations for migratory birds; studies have shown that a J formation is, in fact, more common than a true V-shaped structure.) One way to account for the phenomenon is that followers benefit from a supportive upwash of air created by the lead birds. The other is that regimented flight formation facilitates proper spacing, directional orientation and group communication.

The relative importance of each benefit undoubtedly shifts along with changes in various factors, such as the season of the year or the purpose of an individual flight. During local feeding flights, for example, energy conservation is probably much less important than careful orientation and collision avoidance are. During long-distance migration, on the other hand, each member of the flock gains a great deal by optimizing its position to conserve energy. ■

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

STEVE GSCHMEISSNER *Photo Researchers, Inc. (olfactory neuron);*
HORST NEUMANN *Getty Images (woman sniffing wine);* DLILLC/CORBIS *(geese)*

Does Infinity Come in Different Sizes?

BY JOHN MATSON

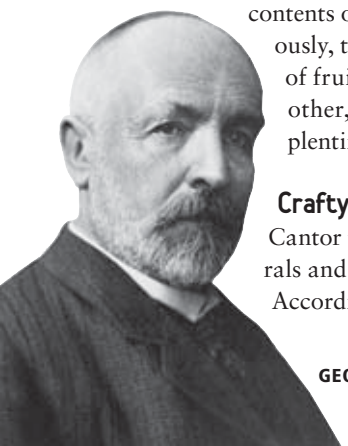
In the 1995 film *Toy Story,* the gung-ho space action figure Buzz Lightyear tirelessly incants his catchphrase: "To infinity … and beyond!" The joke, of course, is rooted in the perfectly reasonable assumption that infinity is the unsurpassable absolute—that there is no beyond. That assumption, however, is not entirely sound. As German mathematician Georg Cantor demonstrated in the late 19th century, a variety of infinities exist—and they can be classified by their relative sizes.

Natural Logic

Take, for instance, the so-called natural numbers: 1, 2, 3, and so on. These numbers are unbounded, and thus the collection, or set, of all the natural numbers is infinite in size. But just how infinite is it? Cantor used an elegant argument to show that the naturals, though infinitely numerous, are actually less numerous than another common family of numbers: the real numbers. This set comprises all numbers that can be represented as a decimal, even if that decimal representation is infinite in length. Hence, pi (3.14159…) is a real number, as is 27 (which is both natural and real).

Cantor's argument used the logic of contradiction: he first assumed that these sets are the same size; next he followed a series of logical steps to find a flaw that would undermine that assumption. He reasoned that if the naturals and the reals have equally many members, then the two sets can be put into a one-to-one correspondence. That is, they can be paired so that every element in each set has one—and only one—"partner" in the other set.

Think of it this way: even in the absence of numerical counting, one-to-one correspondences can be used to measure relative amounts. Imagine two crates of unknown sizes, one of apples and one of oranges. Withdrawing one apple and one orange at a time thus partners the two sets into apple-orange pairs. If the contents of the two crates are emptied simultaneously, the two boxes contain an equal number of fruits; if one crate is exhausted before the other, the one with remaining food is more plentiful.



GEORG CANTOR

Crafty Math

Cantor thus began by presuming that the naturals and the reals are in such a correspondence. Accordingly, every natural number n has a real partner r_n. The reals can then be listed in order of their corresponding naturals: r_1, r_2, r_3, and so on.

Then Cantor's wily side comes out. He created a real number, called p, by the following rule: make the digit n places after the decimal point in p something other than the digit in that same decimal place in r_n. A simple method would be: choose 3 when the digit in question is 4; otherwise, choose 4.

For demonstration's sake, say the real-number partner for the natural number 1 is 27 (or 27.00000…), the pair for 2 is pi (3.14159…) and that of 3 is President George W. Bush's share of the popular vote in 2000 (0.47868…). Now create p following Cantor's construction: the digit in the first decimal place of p should not be equal to that in the first decimal place of r_1 (27), which is 0. Therefore, choose 4, and p begins 0.4…. (The number *before* the decimal can be anything; 0 is used here for simplicity.) Then choose the digit in the second decimal place of p so that it does not equal that in the second decimal place of r_2 (pi), which is 4. Select 3, and now $p = 0.43\ldots$. Finally, choose the digit in the third decimal place of p so that it does not equal the one in the corresponding decimal place of r_3 (President Bush's percentage), which is 8. Write 4 again, making $p = 0.434\ldots$. Thus, you have:

$r_1 = 27.00000\ldots \longrightarrow p = 0.4\ldots$
$r_2 = 3.14159\ldots \longrightarrow p = 0.43\ldots$
$r_3 = 0.47868\ldots \longrightarrow p = 0.434\ldots$

This mathematical method (called diagonalization), continued infinitely down the list, generates a real number (p) that, by the rules of its construction, differs from every real number on the list in at least one decimal place. Ergo, it cannot be on the list.

In other words, for any pairing of naturals and reals, there exists a real number p without a natural-number partner—an apple without an orange. Therefore, any one-to-one correspondence between the reals and the naturals fails, which means that the infinity of real numbers is somehow greater than the infinity of natural numbers. ■

John Matson is a copy editor at Scientific American.

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LOGAN PARSONS (*infinity symbols*); CORBIS (*Cantor*)