BOOSTS FOR VACCINES
The power of adjuvants

ANOTHER CENTURY OF OIL?
Getting more from current reserves

SCIENTIFIC AMERICAN

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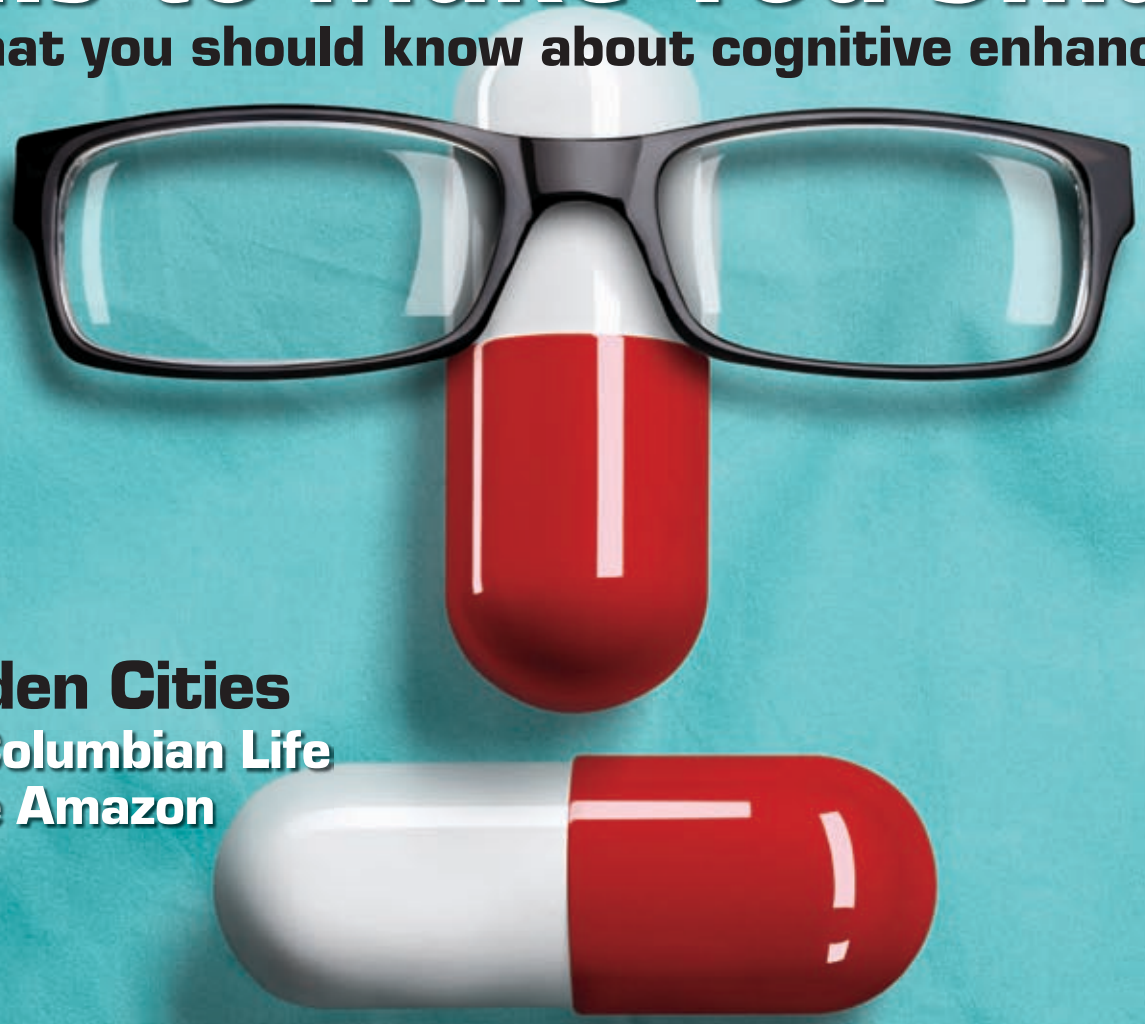
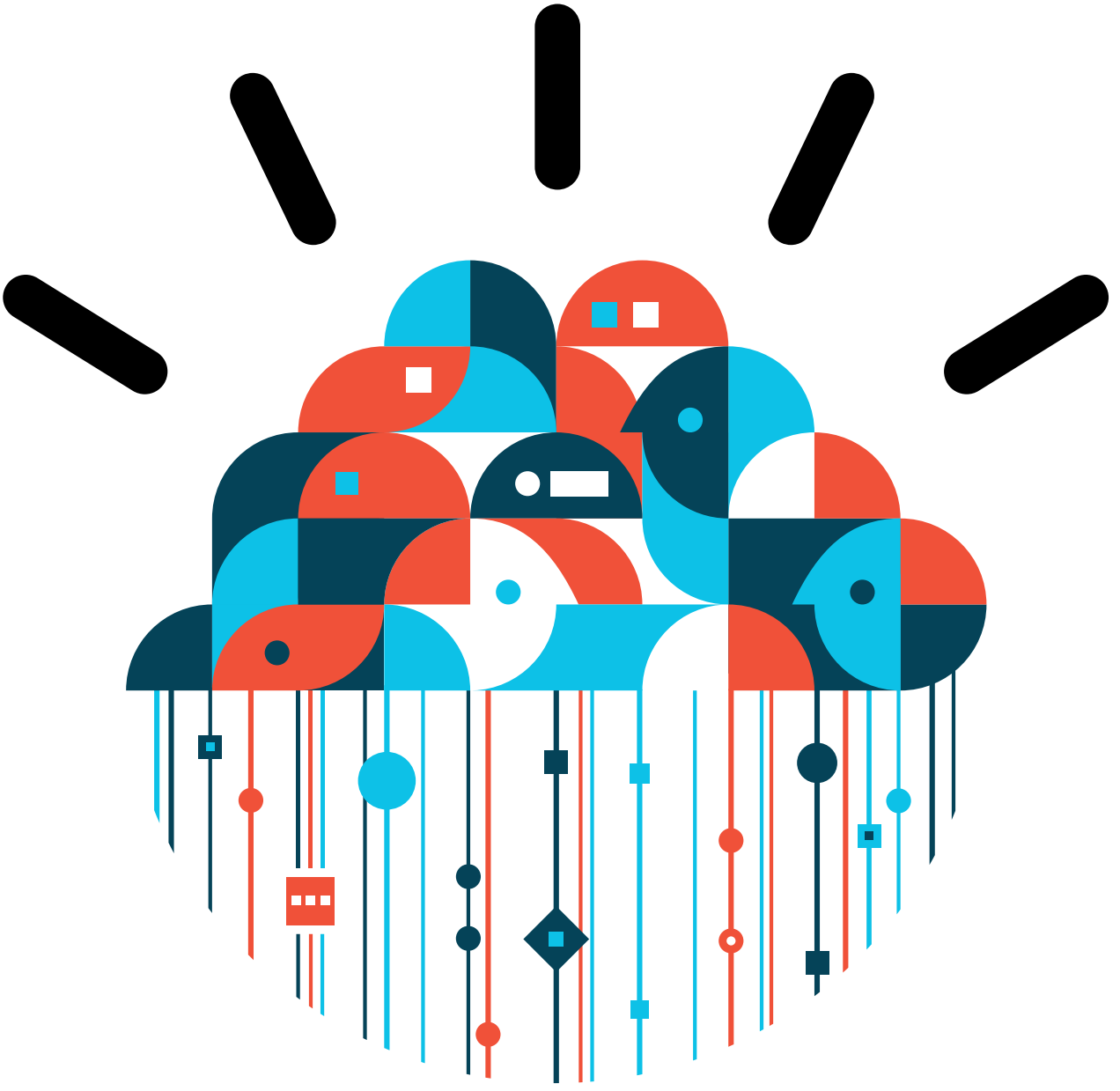
How Quantum Effects Could Create BLACK STARS, Not Holes
page 38

Pills to Make You Smart
What you should know about cognitive enhancers



Plus:

Garden Cities
Pre-Columbian Life in the Amazon



Conversations for a Smarter Planet

Smarter clouds on the horizon.

In previous installments of this ongoing conversation, we have talked about the need for information technology itself to become smarter. Despite enormous advances in computing power, the world's IT infrastructure—already under severe stress from today's computing tasks—could easily become overwhelmed by the onrushing complexity and unprecedented data generated by nearly a trillion instrumented and interconnected devices, objects, processes and people.

Fortunately, help is at hand. It comes in the form of a new model called "cloud computing," in which processing, storage, networking and applications are accessed as services over networks—public, via the Internet; or private, via intranets. It makes possible a new level of system intelligence—also known as "service management"—with the potential to secure, authenticate, customize and just plain keep up with the coming wave of data complexity and volume.

Importantly, just as the clouds above us are differentiated—cirrus, stratus, cumulus—the smart clouds of a smarter planet will develop around particular tasks. They will be optimized for workloads as diverse as software development and virtual desktops, as smarter traffic management and smarter retail.

Some will enable entire business and civic ecosystems to function more smoothly. For instance, consider the city of Wuxi in southeastern China, which developed a "cloud services factory" to provide computing resources to local companies. Software developers can access new resources in minutes, and new businesses can hit the ground running. Wuxi now has the potential to provide services to hundreds of small and medium-sized companies, which represent the future of a city that sees itself as an engine for growth.

Some clouds will extend the capabilities of a smarter planet to communities with limited resources. Thanks to a private education cloud, the 12-year-old computers of the Pike County School System in eastern Kentucky now behave more like 2009 models. This has enabled the county to cut 62% of its schools' end-user support costs, while providing equal access to education content across 27 schools. Most importantly, Pike's 10,000 students can now access new courseware instantly—something that used to take more than a year.

And some clouds will help provide more secure and stable public services when it matters most. Following Hurricane Ike in 2008, Houston was plagued by downed trees and power lines — but the nonprofit human services agency Neighborhood Centers Inc., with its system data backed up in a cloud, didn't suffer a single business disruption at any of its 20 facilities. Following the storm, the agency was back in business, providing support to families in need.

Around the world, IBM is working with banks, telecommunications providers, retail firms, governments and universities to use clouds to optimize for specific economic and societal goals, and to infuse their technology systems with IBM's unique depth of expertise. All because smarter clouds are now gathering on the horizon.

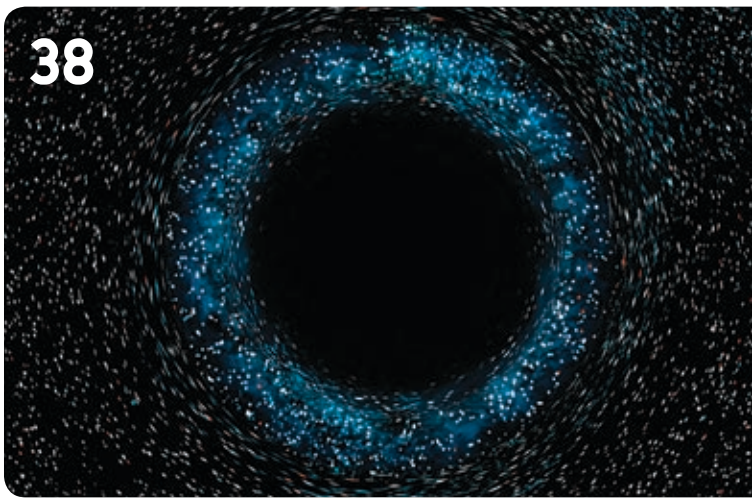
Let's build a smarter planet. Join us and see what others are thinking at **ibm.com**/smarterplanet

Can today's environmental thinking inspire tomorrow's technology? Toyota believes so. Since its launch, the Prius has earned the love of millions of forward-thinking drivers. We estimate our hybrid technology has saved a billion gallons of gas and lowered CO_2 emissions by billions of pounds.* It's also paving the way for the next generation of environmental vehicles. Like cars charged at home. Or cars that will run solely on electricity, or consume hydrogen and emit only water. Because when it comes to thinking green, the sky's the limit.

*Estimated savings compares each U.S. hybrid vehicle's EPA combined mpg rating with its segment average based on latest EPA Trends Report (driven 15,000 miles annually). Actual mileage will vary. ©2009

CONTENTS FEATURES

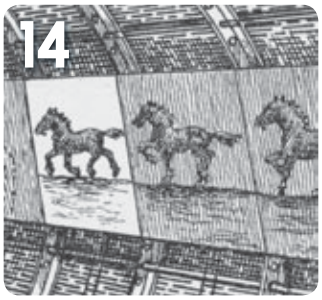
SCIENTIFIC AMERICAN October 2009 ▪ Volume 301 Number 4

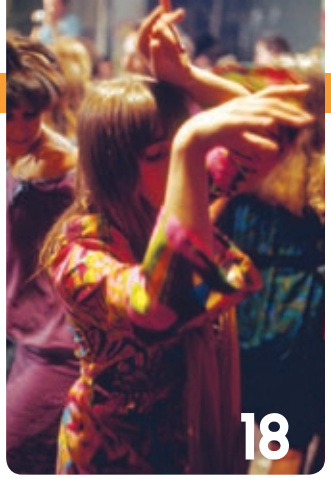


ON THE COVER

Cognitive enhancers, drugs that promise to sharpen focus and memory, have hit the headlines recently. But do they work? And are they a good idea? Image by Aaron Goodman.

CONTENTS DEPARTMENTS





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Robotic Space Exploration
Fifty years after a probe first landed on the moon, we look back at the many achievements of unmanned pioneers, such as the Mars Exploration Rovers (*one depicted here*).

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More at **www.ScientificAmerican.com/oct2009**

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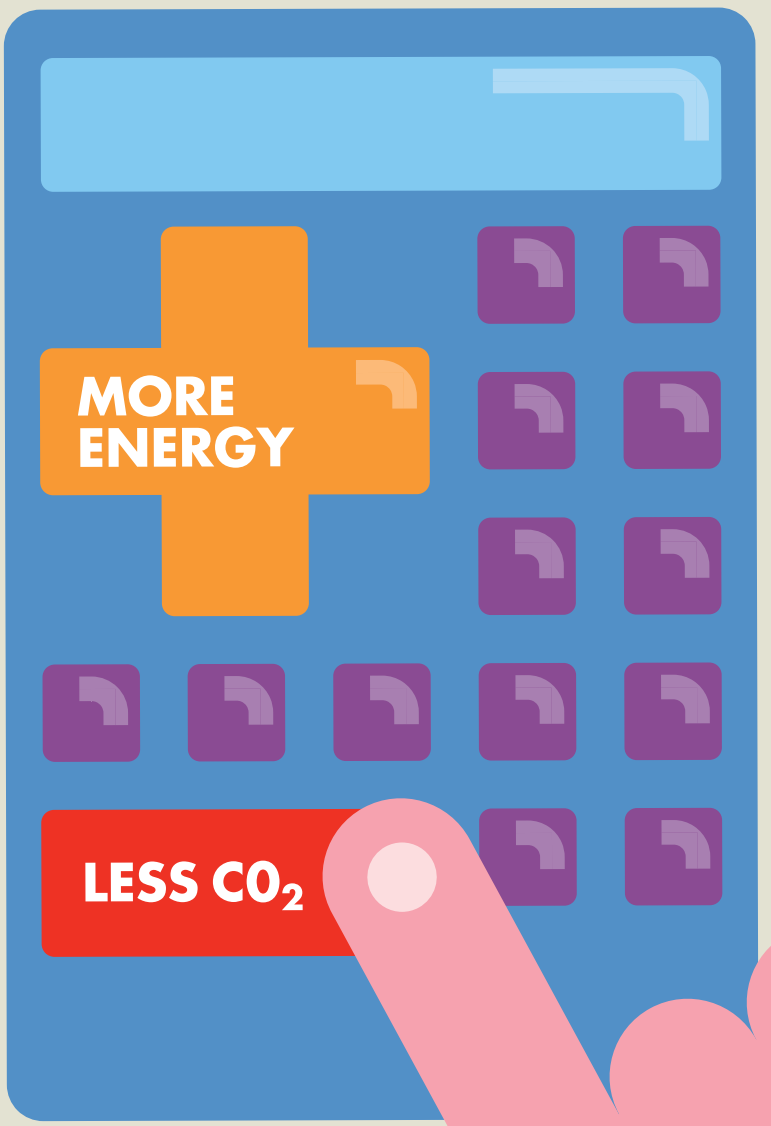
FOR THE NEW ENERGY FUTURE
WE NEED TO MAKE IT ALL ADD UP.



Meeting the growing demand for energy while reducing CO_2 emissions may seem like an impossible equation. But by focusing our efforts in four key areas we're taking positive steps towards a solution.

We continue to help deliver greater energy security with our oil and gas business. We're developing diverse energy sources like biofuels and finding ways to help our customers use energy more efficiently. And we're actively exploring ways to manage CO_2 more effectively, like carbon capture and storage technology.

To find out how Shell is helping prepare for the new energy future visit **www.shell.com/newenergyfuture**

Playing the Averages

"The year was 2081, and everybody was finally equal. They weren't only equal before God and the law. They were equal every which way. Nobody was smarter than anybody else. Nobody was better looking than anybody else. Nobody was stronger or quicker than anybody else."

In the opening of the classic 1961 short story "Harrison Bergeron," novelist Kurt Vonnegut depicted a future in which people who had been born superior in some way over "average" people could not use those gifts to take "unfair" advantage. The strong lugged handicapping weights, the beautiful wore hideous masks and the clever were not permitted to think for stretches longer than 20 seconds or so. "A little mental handicap radio" transmitted earsplitting sounds such as a buzzer, a 21-gun salute or a ball-peen hammer striking a milk bottle. In response, "thoughts fled in panic, like bandits from a burglar alarm."

BETTER BRAINS from a bottle?

Gun-toting government agents enforced the legislated baseline of mediocrity. When dull but well-meaning Hazel suggests that her husband, George, remove a few lead balls from his "handicap bag," he reminds her of the fines and why he mustn't disobey anyway: " 'If I tried to get away with it,' said George, 'then other people'd get away with it and pretty soon we'd be right back in the dark ages again, with everybody competing against everybody else. You wouldn't like that, would you?' " No, she wouldn't.

The must-have standards in the real 2081 will likely differ from Vonnegut's unhappy tale, but the desire to achieve them may be uncomfortably similar. Our society, too, seems to be transfixed by the goal of reaching an average—one that is "above average." With cosmetic surgery, we sculpt our bodies to create an ideal of attractiveness. Athletes dip into the medicine cabinet to pump up muscles and speed. Is it any wonder that recent headlines bark about the possibility of taking pills to boost brainpower?

As senior writer Gary Stix writes in the cover story, "Turbocharging the Brain," older workers feel the need to vie with agile younger minds, students are pressed to make good grades while pulling all-nighters, and multitaskers want to maintain focus. Pills offer a tantalizingly easy solution. But would such drugs actually be an effective means of sharpening thought, and would they be as relatively harmless over the long term as having the occasional cup of coffee? Turn to page 46 for an exploration of the science of enhancing cognition—and the issues that it raises.

While many people reach eagerly for bottled brain improvements, others are wary of medical enhancements—in the form of more potent vaccines—that would benefit overall public health. Nathalie Garçon and Michel Goldman describe new adjuvants, ingredients that help to stimulate the human immune system, in "Boosting Vaccine Power," starting on page 72. But hesitation by the public and policy leaders has slowed acceptance in the U.S., as we explain in Perspectives, on page 30. Our unequal enthusiasms about what is important to improve say much about the choices we make. ■

MARIETTE DiCHRISTINA
acting editor in chief

ETHAN HILL (*DiChristina*); SPLASHLIGHT (*pills*); SCIENTIFIC AMERICAN (*Stix*)

Among Our Contributors

NATHALIE GARÇON
is a pharmaceutical scientist specializing in immunology and is head of the Global Adjuvant Center for Vaccines at GlaxoSmithKline Biologicals.

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is a professor of immunology at the Université Libre de Bruxelles in Belgium. His research centers on factors controlling dendritic cells and Toll-like receptor signaling.

MICHAEL J. HECKENBERGER
is a professor at the University of Florida who studies the Xingu region and other areas of the Brazilian Amazon. He is interested in the organization of late prehistoric societies in the region.

SETH LLOYD
is professor of mechanical engineering at the Massachusetts Institute of Technology. His work focuses on quantum computers and communication schemes.

GARY STIX
is senior writer for *Scientific American*. He writes, solicits and edits articles on neuroscience and a range of other topics. He often serves as issue editor for *Scientific American*'s annual single-topic issue.

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Who Attends

OnDC features the most innovative companies, eminent technologists and scientists, influential investors, public policy makers, and journalists in keynote presentations, panel debates, and private company CEO showcases. Our goal is to identify the most promising entrepreneurial opportunities and investments, and uncover how to best capitalize on top government initiatives.

At OnDC, our editors will also honor the OnDC 100—the private companies that most impact the public sector. Up to 50 technology CEOs will pitch their market strategies to a panel of industry experts in CEO showcase sessions.

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Obama's Science ▪ Phosphorus Bugs ▪ Cats and Rats

JUNE 2009

"Using mineral fertilizers diminishes the abundance and diversity of soil microorganism populations."
—Norman T. Uphoff
CORNELL UNIVERSITY

Tax Dollars at Work

Despite Barack Obama appointing scientists to top posts, I hardly think this qualifies him personally to be named in the "Scientific American 10." His inclusion pales beside the favor bestowed to the others on the list who have actually done some real work for science and humanity.

Catherine McBride-Bergum
Virginia, Minn.

Although your infatuation with Obama is most likely impervious to facts, I would like to point out that federal R&D spending increased 41 percent in inflation-adjusted dollars over the course of the Bush administration. Also, Bush's spending on embryonic stem cell research, though more restricted than you may have liked, represented a rather substantial increase over the Clinton administration, during which embryo-destructive federal research funds were essentially zero. *Scientific American*'s praise should be reserved for those who actually perform the hard work of advancing scientific knowledge, not those who merely allocate money they did not earn to researchers they will never meet.

Greg Pitner
Austin, Tex.

Soil Welfare

David A. Vaccari's "Phosphorus: A Looming Crisis" usefully called attention to the critical role of phosphorus as a plant and crop nutrient and to possible future scarcities and constraints. But his focus on it as a fertilizer neglected its abundance in most soils. There is usually 10, 20, sometimes even 30 times more phosphorus in the soil than the amount in "available" forms that plants can readily utilize. The large amount of unavailable phosphorus is continuously, though relatively slowly, converted into available forms through the activity of soil microorganisms, many of which are known as phosphobacteria.

Without these microorganisms, plants could not have been growing in the earth's soils for more than 400 million years. Ironically, the use of inorganic fertilizers can suppress roots' and microorganisms' production of the phosphatase enzymes that are essential for making phosphorus available for plant use. This inhibition is similar to the way that adding inorganic nitrogen to the soil diminishes the production of nitrogenase by plants and microorganisms to sustain their fixation of atmospheric nitrogen, which becomes available for plant nutrition.

Heavy machinery also compacts the soil and degrades its structure, disturbing the balance of water and air in the soil that supports root growth and soil organisms; further, using mineral fertilizers as a substitute for restoration of soil organic matter diminishes the abundance and diversity of soil microorganism populations.

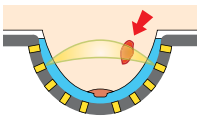
It is true that under a variety of conditions, applications of phosphorus fertilizer and rock phosphate in particular can be beneficial and cost-effective. But from a sustainable agriculture perspective, more

In the future, new optical techniques may complement traditional mammograms...

A unique type of mammogram

Getting regular mammograms is very important. But women have long hoped for an easier way to get them. So, Hamamatsu is working to develop a unique new type of mammogram...

One that uses *light* instead of x-rays. And *no breast compression*. A woman simply lies face down on a table and suspends her breast into a cup of warm liquid for maximum comfort.

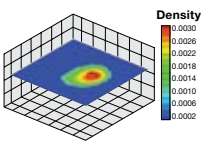


Shining near-infrared light through the breast can identify tumor locations.

Lining that cup is an array of tiny modules that shine near-infrared light at the breast—and then precisely sense the light that passes through.

By applying unique algorithms to that data, varying with the type of cancer, Hamamatsu is actually able to identify tumors in the breast.

This new principle works by measuring subtle increases in blood volume from the new blood vessels generated by breast cancers. It can even spot changes in tissue structure.



A sliced optical mammogram image from preliminary testing reveals high-density tumor area (red).

For the future, for screening and investigation of breast cancer and as a potential complement to traditional mammograms, Hamamatsu's optical mammography is showing great promise.

For the women of the world, it will be a very welcome development!

http://jp.hamamatsu.com/en/rd/publication/

Hamamatsu is opening the new frontiers of Light

HAMAMATSU

Photon is Our Business

Photograph Courtesy of the NAIC - Arecibo Observatory, a facility of the NSF

▲ Explore the contributions and potential of radio astronomy at the celebrated Arecibo Observatory. Get an unparalleled behind-the-scenes tour of the iconic facility, and absorb an in-depth look at the unique contributions derived from Arecibo research and development.

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Refresh your science spirit with the vitality of intelligent conversation, the balance of conceptual and practical, and the energy of striving towards new horizons. Join Scientific American on Bright Horizons 6 cruise conference on Holland America's Eurodam, December 5–12, 2009. Expert knowledge, lush Caribbean islands, recreation and reflection await you.

Update your cosmology knowledge with Dr. Lawrence Krauss, as he analyzes which cosmology ideas and theories are holding up over time, which have changed, and which suggest the future form of the universe. Tune in to astronaut Dr. Guy Bluford and learn first hand about Space Shuttle and International Space Station missions. Rendezvous with Dr. Jim Bell and make a deep impact on your knowledge of Near Earth Asteroids and planetary geology. Think green and dig in to a hot topic with Dr. David Blackwell, geothermal energy maven. Sit with immunologist Dr. Noah Isakov and get the latest thinking in allergy, immunobiology, and the origins of cancer.

Take home keys to understanding pressing topics in green energy, medicine, and space science. Savor the moment with a friend on an uncrowded Grand Turk beach or a Virgin Islands rainforest hike.

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Cruise prices vary from $799 for an Inside Cabin to $2,999 for a Full Suite, per person. (Cruise pricing is subject to change.) For those attending the conference, there is a $1,375 fee. Optional eight-hour Arecibo Observatory tour is $175 and includes transportation, entrance fees, and luncheon. Taxes and gratuities are approximately $150.

Einstein's Big Blunder, A Cosmic Mystery Story
Speaker: **Lawrence Krauss, Ph.D.**

A review of the revolutions that have taken place in cosmology over the past decade, including the discovery of Dark Energy, which permeates space and drives cosmic expansion. Tune in to Dr. Krauss and develop a deeper understanding of space, time, and gravity — one that is apt to change your picture of the universe.

The Undiscovered Country
Speaker: **Lawrence Krauss, Ph.D.**

We humans have undoubtedly questioned the origins of the cosmos for as long as we've walked the Earth but we've made spectacular progress in recent years. This progress forces us to discard much of what cosmology textbooks told us up until quite recently. Get the latest on competing ideas, their implications, and how they can be experimentally tested.

Postcards from Mars
Speaker: **Jim Bell, Ph.D.**

The NASA Mars Exploration Rovers Spirit and Opportunity landed on the Red Planet in January 2004, and have been driving, photographing, and analyzing their landing sites for the past five years. Prof. Bell has been the lead scientist in charge of the rovers' Panoramic Camera imaging system since the rovers were "born" nearly a decade ago. Come along for an amazing journey of geologic exploration and learn about the ways that both rovers have been utilized to discover convincing evidence that Mars was once warmer, wetter, and much more Earthlike than it is today.

Studying the Solar System in 3-D
Speaker: **Jim Bell, Ph.D.**

Don your red-blue glasses and join planetary imaging expert Prof. Jim Bell on a voyage of 3-D discovery of the solar system. Stereo pictures of Mars, the Moon, Saturn, asteroids, comets, and other places taken by astronauts and robotic space probes provide new details about the geology and history of our planetary neighbors. Learn about the ways that 3-D images are taken, and the ways that they are used by scientists and engineers involved in space exploration. Viewing the solar system in 3-D is the next best thing to being there!

Listed is a sampling of the 20 sessions you can participate in while we're at sea. For a full listing visit
www.InSightCruises.com/SciAm6-talks

Plate Tectonics
Speaker: **David D. Blackwell, Ph.D.**

Glide into an updated understanding of plate tectonics. Join Dr. Blackwell for a discussion of the development of the theory, its key principles, and its consequences. You'll learn about physical properties of the dynamic lithosphere, athenosphere, and mantle layers versus chemical layers of the earth, driving forces of plate movement, and the relationship of plate boundaries to geological events such as earthquakes and the creation of topographic features like mountains, volcanoes, and oceanic trenches.

The Space Shuttle Program
Speaker: **Guion S. Bluford, Jr., Ph.D.**

Countdown to contemporary treasure – a first-hand account of life in space. Dr. Guion Bluford, a veteran of four Space Transportation System (STS) missions (STS 8, STS 61-A, STS 39, and STS 53) will present a look at the Space Shuttle Program, from its inception to the wrap up of its service in 2010. Learn about training for shuttle duty, noteworthy aspects of daily routine in space on the Discovery and Challenger, and gain a behind the scenes look at the science and technology projects executed by Shuttle astronauts.

The International Space Station
Speaker: **Guion S. Bluford, Jr., Ph.D.**

Join Dr. Bluford for a comprehensive survey of the International Space Station (ISS) Program. He will orient us to the history and complexities of this permanent human presence in space. From project inception to launch to ongoing development and daily living, pick up a new understanding of the logistics, function, and significance of the ISS.

The Future of the Space Program
Speaker: **Guion S. Bluford, Jr., Ph.D.**

Travel back to the future with an indepth discussion on the future of the NASA Space Program. Dr. Bluford will address the issues and opportunities ahead as space exploration matures. You'll get the big picture of the Constellation Program (with its Aries, Orion, and Altair components) which will return humans to the moon and later take them to Mars. Come away with the insights and views on what lies ahead from Dr. Bluford, astronaut and aeronautical engineer.

Monoclonal Antibodies and Cancer Immunotherapy
Speaker: **Noah Isakov, Ph.D.**

Take a look under the hood of contemporary immunotherapy. From molecular biology to medicine, monoclonal antibodies are a valuable part of the scientist's toolkit. From his view deep in the trenches of immunobiology, Dr. Isakov will offer:

- An overview of antibody molecules
- A guide to the production of monoclonal antibodies with specificity against a predetermined pathogen
- The scoop on monoclonal antibody use in research, diagnosis, and therapy

For details contact: Neil Bauman
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Partake of intellectual adventure in the company of experts and fellow citizens of science. Join Scientific American Travel on a cruise down the mighty St. Lawrence Seaway into the heart of contemporary cosmology, genetics, and astronautics. Black holes parallel universes, and the Big Bang itself are among the abstract ports of call Dr. Max Tegmark shows us. You'll have a new perspective on the significance of food choices after indulging in a discussion with Dr. Paul Rozin. Satisfy your curiousity about navigating space, from the science behind solar sails to mapping the Interplantetary Superhighway, with Dr. Kathleen Howell. Maneuver through the newly charted territory of the human genome, genetic medicine, genetic agriculture, and all their nuances and consequences with Dr. David Sadava. Set the scene for Summer on the Bright Horizons 7 conference on Holland America Line's m.s. Maasdam, sailing Montreal to Boston May 29-June 5, 2010.

Cap your Bright Horizons experience with an optional, incomparable, behind-the-scenes tour of the Massachussetts Institute of Technology with MIT insider Dr. Max Tegmark as your guide. Campus, research facilities, and lunch at the MIT Museum are on the itinerary. ▼

Discover the pleasures of dynamic and interactive science learning in Canada's historic and hospitable Atlantic provinces, and bring back your own True North story. Hike Springtime Quebec with a friend. Hear Celtic echoes in the Nova Scotia breeze. Visit www.insightcruises.com/SciAm-8 or call Neil or Theresa at (650) 787-5665 to get all the details, and then journey with Scientific American and a thinking community on Bright Horizons.

How Did It All Begin — Or Did It? How Will It All End?

Although we humans have undoubtedly asked these questions for as long as we've walked the Earth, we've made spectacular progress on them in recent years, forcing us to discard much of what cosmology textbooks told us up until quite recently. Get the latest on competing ideas, their implications and how they can be experimentally tested.

Questions, I've Got Questions: Black Holes Edition

Take a look at some of the most spectacular recent evidence that black holes really exist. Dr. Tegmark will cover what we know about them and what remains mysterious. Are black holes in fact crucial to enable galaxies to form? Can black holes form new universes in their interiors? Plus, using a fully general-relativistic flight simulator, you'll take a scenic orbit of the monster black hole at the center of our Galaxy and discuss how one could actually make this dizzying journey with only modest energy expenditure.

A Brief History of Our Universe

With a cosmic flight simulator, we'll take a scenic journey through space and time. After exploring our local Galactic neighborhood, we'll travel back 13.7 billion years to explore the Big Bang itself and how state-of-the-art measurements are transforming our understanding of our cosmic origin and ultimate fate.

Mission Design: Exploring the Solar System

Scientific mysteries and huge surprises await all of us space explorers, whether we're viewing Earth from the perspective of space or seeking out our neighbors, that is, the planets, dwarf planets, moons, asteroids, and comets that populate the solar system. But how do we get there? How do we get a spacecraft where we want it to go? What about power? How do we address the demands of the space environment? Dr. Howell will lay out the principles and process of designing a space mission. Get the scoop on the successful engineering techniques and some of the challenges in getting humans and robots to space destinations.

Solar Sailing

Nearly 400 years ago, Johannes Kepler observed that the tails of comets are sometimes blown about what he considered to be a solar "breeze." Kepler suggested that perhaps ships could move through space using large sails to capture the breeze from the Sun. The concept of practical solar sailing was introduced in the 1920's and serious studies of the idea by engineers began in the 1950's. Solar sails are very thin sheets of reflective material that reflect sunlight — they transfer the momentum of light energy to their spacecraft. This sunlight pressure yields a force that pushes a spacecraft through space, without using any fuel. Solar sails are real! Test sails are being constructed; solar sail capabilities are being analyzed; solar sail mission have been planned. Learn the facts with Dr. Howell.

Genetic Medicine: Can knowledge of the genome transform medicine?

Your health is determined by both heredity and environment. Beginning in the 1800s, humankind has made great progress in modifying the environment to improve public health. This progress has led to the near-elimination of many infectious diseases in some parts of the world and treatments for other diseases. Dr. Sadava will show you that as we learn more about our heredity through studies of the genome, we can describe what goes wrong in the many diseases that have a genetic component, such as cancer and heart disease. Get a researcher's input on how these descriptions may lead to cures and how information about an individual's genome may lead to personalized treatments.

Cloning and Stem Cells: What are the potential uses of plant, animal and human cloning and what is the reality of stem cell uses?

The biology behind cloning has been known for over a century. The first plant was cloned in the mid-1950s and the first animal several decades later. In this lecture, you will learn how and why these feats were accomplished. Human cloning is now a possibility. The promise of using stem cells to treat diseases and even improve athletic performance in healthy people is a related topic. Delve into the realm of cloning and stem cells with Dr. Sadava. You'll learn of the ethical issues surrounding the use of human embryos to get the cells used, and the ways biologists may circumvent these concerns.

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attention should be paid to managing the soil biota along with crops so as to get the most benefit from the latter.

Norman T. Uphoff
Professor of Government and International Agriculture
Cornell University

Gregarious Cats

"The Taming of the Cat," by Carlos A. Driscoll, Juliet Clutton-Brock, Andrew C. Kitchener and Stephen J. O'Brien, is largely unsubstantiated and erroneous with regard to the social behavior of domestic cats. Cats do live in groups if the opportunity is available, and each group has a female matriarch and an alpha male. Feral cats always form groups, which are referred to as colonies, and people who care for numerous cats all report this type of hierarchy. As for the cats being of no particular benefit, the authors should consider what species controls the more than 40 eggs laid by many species of snakes, not to mention rodents, whose only other predators are birds of prey and opossums.

"Gary in Tampa"
via ScientificAmerican.com

LONER? Feral cats can be social or solitary, depending on their sources of food.

DRISCOLL REPLIES: *A particular sentence seems to have caused confusion, one where we write: "Cats, in contrast, are solitary hunters." What should have appeared in print is the more specific: "Wildcats, in contrast, are solitary hunters." The social structure of feral cats is heavily influenced by resource availability. Unless they are feeding from a point source (perhaps a kind person or a garbage dump), feral cats sourcing their own food are solitary. Yet even well-socialized cats do not achieve the level of sociality seen in lions, which hunt cooperatively.*

As for their benefits, cats have never been bred for any "behavior" in the sense of a utilitarian task such as shepherding, retrieving, guarding or even pulling, as some domestic dogs were.

It has been suggested that the plagues afflicting Europe during the Middle Ages are a consequence of a reduction in cat numbers during that time and a supposed rise in rat numbers. But humans' susceptibility at the time had more to do with the Little Ice Age and the Great Famine—with resulting changes in socioeconomic structure, living patterns and hygiene—and also with the prevalence of the black rat, Rattus rattus. *The plagues ended after the climate improved, promoting a restoration of agricultural productivity and more dispersed living quarters. Perhaps most important, the black rat was displaced by the brown rat (*R. norvegicus*), which is not as susceptible to infection. The inability of cats to control plague is anecdotally highlighted by noting that the plague also struck places where cats were always in high density.*

CLARIFICATIONS In writing about Todd Brady ["Scientific American 10"], Melinda Wenner says, "Since 2001 Intel has saved more than 500 million kilowatt-hours of energy, enough to power more than 50,000 homes." The figure refers to the energy usage of 50,000 homes for one year.

In "Where the Fault Lies within a Plate," by Charles Q. Choi [News Scan], Seth Stein is quoted as saying, "Perhaps the most damaging earthquake in Australia's recent history was in Newcastle in 1989.... It was in the middle of the continent." Newcastle is on the coast; it is, however, on continental crust in the middle of the Australian plate.

ERRATUM In "The Price of Silent Mutations," by J. V. Chamary and Laurence D. Hurst, in the codon–amino acid table on page 49, the correct name is phenylalanine, not phenylanaline.

Letters to the Editor

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Compiled by Daniel C. Schlenoff

OCTOBER 1959

FOUNDER OF KIDNEY TRANSPLANTS—"Identical-twin grafts have demonstrated that where an immunological barrier does not exist kidneys can be successfully transplanted to cure otherwise incurable kidney and vascular disease. We transplanted a kidney from a healthy man to his critically uremic brother. Though the men were probably not identical twins, we hoped that their relationship might make for some immunologic compatibility. The recipient was given a total dose of X-rays large enough to depress his reticuloendothelial tissues severely. As the patient's reticuloendothelial system recovers from the radiation, it may be forced to become familiarized with the antigens and the transplanted kidney. It is as yet too early to evaluate the results of this transplant, but initially it appears to be successful. —John P. Merrill"

OCTOBER 1909

ELECTROCULTURE—"The rapid growth of plants in the polar regions has hitherto been attributed to the continuous daylight of two or three months in summer, but this explanation must be abandoned. Prof. Lemstroem, of the University of Helsingfors, Finland, finds several reasons for believing that the cause of rapid growth in the Arctic is to be found in the electrical currents which flow between the earth and the atmosphere, and produce the phenomena of the aurora borealis. The pointed leaves of conifers and the barbs of ears of grain facilitate the transmission of these currents through those plants, and this function supplies a reason for the existence of these peculiarities."

SUBWAY ENTERTAINMENT—"Moving pictures are produced, as is well known, by a film traveling with intermittent motion before a projector or lantern which throws successive views on the screen. The same results could be obtained if the pictures were stationary and the audience itself were in motion, so as to view the pictures successively. An ingenious inventor has hit upon this scheme to relieve the monotony of subway travel. He proposes to mount a continuous band of pictures at each side of the subway, and have these pictures successively illuminated, by means of lamps placed behind them. The accompanying illustration indicates the method of accomplishing this result."

➥ The "Masstransiscope," installed in the New York City subways in September 1980, uses this zoetropic effect. Videos are available on Google and YouTube.

OCTOBER 1859

FRANKLIN'S REMAINS—"The expedition fitted out two years ago, to search for Sir John Franklin in the Arctic regions, has returned with full and correct tidings of the sad fate of Franklin and his companions. Captain Robert McClintock found the record and remains of Franklin at Point Victory; and it seems that he died in June, 1847—about 11 years ago. The whole of his companions also perished in those inhospitable and desolate regions. We hope the last expedition to these dread solitudes of ice and snow has been made. A north-west passage was discovered by Captain McClure; but of what value is it? For the purposes of navigation, it is perfectly impracticable; and the conclusion is, that the life and treasure which have been expended in Arctic expeditions have been wasted."

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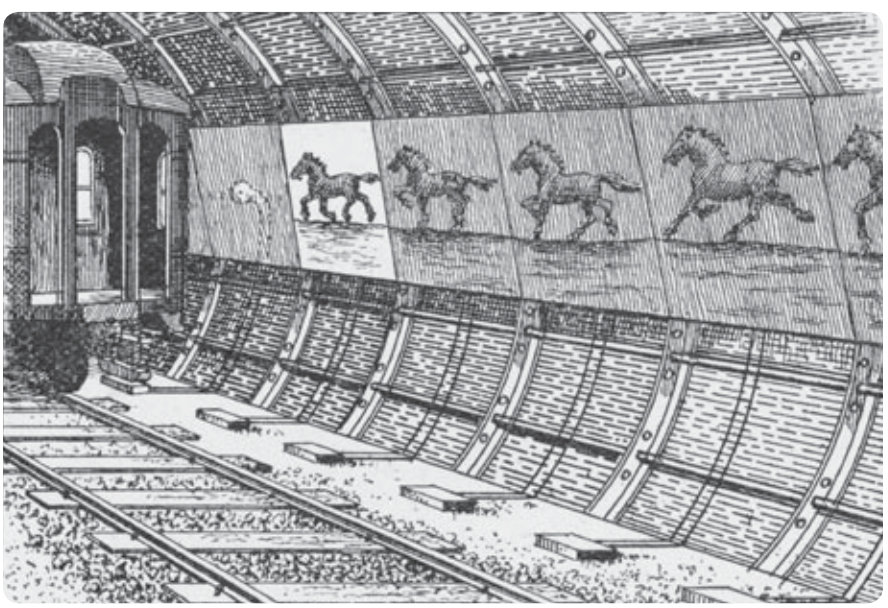

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SCIENTIFIC AMERICAN, VOL. CI, NO. 18; OCTOBER 30, 1909

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Medicine & Health

Return of a Problem Child

LSD makes a comeback as a possible clinical treatment BY GARY STIX

Albert Hofmann, the discoverer of LSD, lambasted the countercultural movement for marginalizing a chemical that he asserted had potential benefits as an invaluable supplement to psychotherapy and spiritual practices such as meditation. "This joy at having fathered LSD was tarnished after more than ten years of uninterrupted scientific research and medicinal use when LSD was swept up in the huge wave of an inebriant mania that began to spread over the Western world, above all the United States, at the end of the 1950s," Hofmann groused in his 1979 memoir *LSD: My Problem Child*.

For just that reason, Hofmann was jubilant in the months before his death last year, at the age of 102, when he learned that the first scientific research on LSD in decades was just beginning in his native Switzerland. "He was very happy that, as he said, 'a long wish finally became true,' " remarks Peter Gasser, the physician leading the clinical trial. "He said that the substance must be in the hands of medical doctors again."

The preliminary study picks up where investigators left off. It explores the possible therapeutic effects of the drug on the intense anxiety experienced by patients with life-threatening disease, such as cancer. A number of the hundreds of studies conducted on lysergic acid diethylamide-25 from the 1940s into the 1970s (many of poor quality by contemporary standards) delved into the personal insights the drug supplied that enabled patients to reconcile themselves with their own mortality. In recent years some researchers have studied psilocybin (the active ingredient in "magic mushrooms") and MDMA (Ecstasy), among others, as possible treatments for this "existential anxiety," but not LSD.

Gasser, head of the Swiss Medical Society for Psycholytic Therapy, which he joined after his own therapist-administered LSD experience, has only recently begun to discuss his research, revealing the challenges of studying psychedelics. The $190,000 study approved by Swiss medical authorities, was almost entirely funded by the Multidisciplinary Association for Psychedelic Studies, a U.S. nonprofit that sponsors research toward the goal of making psychedelics and marijuana into prescription drugs. Begun in 2008, the study intends to treat 12 patients (eight who will receive LSD and four a placebo). Finding eligible candidates has been difficult—after 18 months only five patients had been recruited, and just four had gone through the trial's regimen of a pair of all-day sessions. "Because LSD is not a usual treatment, an oncologist will not recommend it to a patient," Gasser laments.

The patients who received the drug found the experience aided them emotionally, and none experienced panic reactions or other untoward events. One patient, Udo Schulz, told the German weekly *Der Spiegel* that the therapy with LSD helped him overcome anxious feelings after being diagnosed with stomach cancer, and the experience with the drug aided his reentry into the workplace.

TED STRESHINSKY *Corbis*

HAVE A NICE TRIP: The counterculture popularity of the hallucinogen LSD sidetracked research on its possible medical uses for decades.

The trials follow a strict protocol—"all LSD treatment sessions will begin at 11 a.m."—and the researchers are scrupulous about avoiding mistakes that, at times, occurred during older psychedelic trials, when investigators would leave subjects alone during a drug session. Both Gasser and a female co-therapist are present throughout the eight-hour sessions that take place in quiet, darkened rooms, with emergency medical equipment close at hand. Before receiving LSD, subjects have to undergo psychological testing and preliminary psychotherapy sessions.

Another group is also pursuing LSD research. The British-based Beckley Foundation is funding and collaborating on a 12-person pilot study at the University of California, Berkeley, that is assessing how the drug may foster creativity and what changes in neural activity go along with altered conscious expe-

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rience induced by the chemical. Whether LSD will one day become the drug of choice for psychedelic psychotherapy remains in question because there may be better solutions. "We chose psilocybin over LSD because it is gentler and generally less intense," says Charles S. Grob, a professor of psychiatry at the University of California, Los Angeles, who conducted a trial to test psilocybin's effects on anxiety in terminal cancer patients. Moreover, "it is associated with fewer panic reactions and less chance of paranoia and, most important, over the past half a century psilocybin has attracted far less negative publicity and carries far less cultural baggage than LSD."

Others assert the importance of comparative pharmacology—how does LSD differ from psilocybin?—because of the extended period of research quiescence. Just because many types of so-called SSRI antidepressants exist, "it doesn't mean that they are all identical," observes Roland Griffiths, a Johns Hopkins University researcher who conducts trials with psilocybin. In any case, on the 40th anniversary of the Woodstock music festival, psychoactive substances that represented the apotheosis of the counterculture lifestyle are no longer just hippie elixirs.

Nuclear Architecture

Positions inside the cell nucleus exert biological effects BY MELINDA WENNER

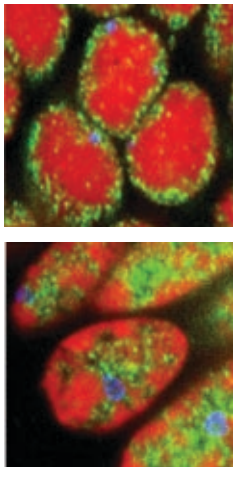
FOR DECADES THE CELL NUCLEUS HAS BEEN A BLACK BOX OF biology—scientists have understood little about its structure or the way it operates. But thanks in part to new visualization technologies, biologists have recently begun probing the architecture of the nucleus in real time. And they are discovering that this architecture appears to change as we age or fall ill or as our needs shift. In fact, the structure of nuclear components—chromosomes, RNA, protein complexes and other small bodies—could be as biologically important as the components themselves.

It is not surprising that the nucleus is carefully organized. The human genome's 3.2 billion DNA base pairs have to be compacted 400,000-fold to fit within the tiny space—yet genes must also interact with one another there and with the machinery that transcribes them into proteins. Nuclear structure has historically been difficult to study because scientists had to rely on electron microscopy or antibody stains, which show cellular components only at single points in time. In the 1990s, however, biologists started using green fluorescent protein to observe nuclear components in living cells in real time, much like a movie. "A picture is worth 1,000 words, and I always like to say a movie is worth one million words," says David L. Spector, a cell biologist at Cold Spring Harbor Laboratory.

One of first things biologists noticed was that genes reside in different parts of the nucleus depending on their activity. Chromosomal regions containing silent genes localize to condensed DNA regions in the outer periphery, whereas active genes stay in the roomier nuclear center, perhaps because there they can more easily share the transcription resources. But "like most things in biology, people have found exceptions," notes Tom Misteli, a cell biologist at the National Cancer Institute. Sometimes active genes are on the periphery, and vice versa.

Chromosomes position themselves carefully relative to one another, too. Mouse olfactory cells contain the genes for 1,300 types of smell receptors, but only one of the genes turns on in each cell. In a 2006 paper researchers used fluorescent tags to show that a receptor gene becomes expressed only if it comes into physical contact with a specific part of chromosome 14. The idea is that "these two chromosomes come together in three-dimensional space, they kiss, and that's how you get your regulation" of genetic activity, Misteli says. Chromosome "kissing" also appears to play a role in determining which X chromosome gets turned off in female cells, because only one copy is usually active.

Changes to nuclear structure can affect cellular function in dramatic ways. In April biologists Thomas Cremer and Boris Joffe of the Ludwig-Maximilians University in Munich noticed that the architecture of retina rod nuclei is inverted in nocturnal mice—condensed DNA sits at the center, with less condensed regions in the periphery. They had no idea why but eventually "came to the incredible idea that it might be related to vision," Joffe says. The researchers compared the retinal nuclei of 38 species and found that those of nocturnal and crepuscular species—animals active at dusk or dawn—featured the inverted structure, whereas diurnal species had the more traditional layout. The inverted architecture seems to minimize light scattering, which allows them to see better in the dark, Joffe says, but it is unclear why.



BUNDLES OF GENES for vision (*green*) cluster on the edges of the nucleus in rats (*top*), which are nocturnal, but reside deeper in the nucleus in chipmunks (*bottom*), which are active during the day.

Aging and disease are also associated with changes to nuclear architecture. Generally, as cells age, stores of condensed DNA at the nuclear periphery start migrating inward. In a study in the *Journal of Cell Biology* in 2008, Misteli and his colleagues identified four cancer-related genes that change positions when breast cells become cancerous. Structure can also influence risk; when chromosomes get too close to one another, cancer-causing chromosomal translocations occur more often. And bizarrely, the X chromosome moves closer to the center after epileptic seizures.

"NUCLEAR ARCHITECTURE OF ROD PHOTORECEPTOR CELLS ADAPTS TO VISION IN MAMMALIAN EVOLUTION," BY IRINA SOLOVEI, MORITZ KREYSING, CHRISTIAN LANCTÔT, SÜLEYMAN KÖSEM, LEO PEICHL, THOMAS CREMER, JOCHEN GUCK AND BORIS JOFFE, IN *CELL*, VOL. 137, NO. 2, APRIL 17, 2009

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No one knows whether these kinds of changes to nuclear structure trigger aging and disease or result from them, or both. In any case, it is clear "that if you mess around with the [nuclear] architecture, you can get disease," Misteli says. It might one day be possible to diagnose diseases and age-related problems simply by looking at nuclear snapshots, he adds.

Perhaps the biggest remaining mystery is how the nucleus gets organized in the first place. Do molecular scaffolds tether nuclear constituents in a deterministic way, or does genome activity affect positioning in a probabilistic manner? Evidence supports both theories, and Spector posits that RNA may play an important role. This past March he and his colleagues identified an RNA that helps to structure nuclear compartments called paraspeckles. Undoubtedly, the mechanisms controlling nuclear organization will prove to be varied and complex. As Spector puts it: "Things in biology tend to not be in black and white."

Melinda Wenner is based in New York City.

Technology

Tasting the Light

Device lets the visually impaired "see" with their tongues BY MANDY KENDRICK

The late neuroscientist Paul Bach-y-Rita hypothesized in the 1960s that "we see with our brains not our eyes." Now a noninvasive device trades on that thinking and aims to partially restore the experience of seeing for the visually impaired by relying on the nerves on the tongue's surface to send light signals to the brain.

First demonstrated in 2003 by neuroscientists at Middleton, Wis.–based Wicab (a company co-founded by Bach-y-Rita), the device could finally be ready for sale at the end of the year. Called BrainPort, it tries to substitute for the two million optic nerves that transmit visual signals from the retina to the brain's primary visual cortex. Visual data are collected through a small digital video camera mounted on the center of sunglasses worn by the user. Bypassing the eyes, the data go to a handheld base unit, which houses such features as zoom control and light settings as well as a central processing unit (CPU), which converts digital signals into electrical pulses.

From the CPU, the signals are sent to the tongue via a "lollipop," an electrode array about nine square centimeters that sits directly on the tongue, which seems to be an ideal organ for sensing electric current. (Saliva is also a good conductor.) Moreover, the tongue's nerve fibers are densely packed and are closer to the surface relative to other touch organs. The surfaces of fingers, for example, are covered with a layer of dead cells called the stratum corneum.

Each electrode on the lollipop corresponds to a set of pixels. White pixels yield a strong electrical pulse, whereas black pixels translate into no signal. The nerves at the tongue surface receive the incoming electrical signals, which feel a little like Pop Rocks or champagne bubbles to the user.

Typically within 15 minutes of using the device, blind people can begin interpreting spatial information via BrainPort, says William Seiple, research director at the nonprofit vision health care and research organization Lighthouse International. The electrodes spatially correlate with the pixels so that if the camera detects light fixtures in the middle of a dark hallway, electrical stimulations will occur along the center of the tongue. "It becomes a task of learning, no different than learning to ride a bike," says Wicab neuroscientist Aimee Arnoldussen, adding that the "process is similar to how a baby learns to see. Things may be strange at first, but over time they become familiar."

COURTESY OF WICAB

TASTE SENSATION: In a device called BrainPort, a sunglasses-mounted camera sends data to a handheld unit, which converts light to electrical signals that can be detected by the tongue.

Seiple works with four patients who are training with BrainPort once a week. He notes that his patients have learned how to quickly find doorways and elevator buttons, read letters and numbers, and pick out cups and forks at the dinner table without having to fumble around. "At first, I was amazed at what the device could do," he says. "One guy started to cry when he saw his first letter." The researchers have yet to figure out if the electrical information is transferred to the brain's visual cortex, where sight information is normally sent, or to its somato-

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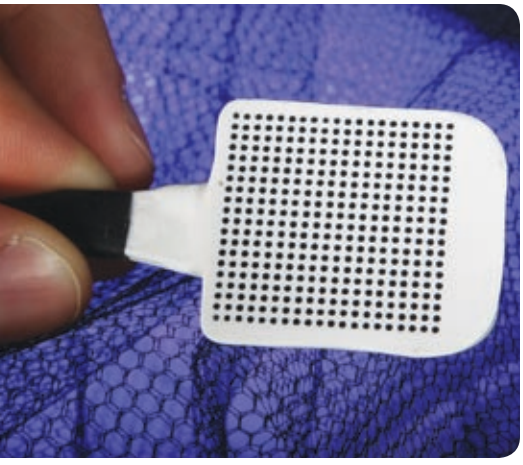
sensory cortex, where touch data from the tongue are interpreted.

To develop criteria for monitoring the progress of artificial sight, optometrist Amy Nau of the University of Pittsburgh Medical Center's Eye Center will further test BrainPort, along with other devices such as retinal and cortical implant chips. "We can't just throw up an eye chart. We have to take a step back and describe the rudimentary precepts that these people are getting," she says. Nau is particularly interested in BrainPort because it is noninvasive, unlike implants.

"Many people who have acquired blindness are desperate to get their vision back," she points out. According to the National Institutes of Health, at least one million Americans older than 40 are legally blind, with vision that is 20/200 or worse or that has a field of view of less than 20 degrees. Adult vision loss costs the country about $51.4 billion a year.



"LOLLIPOP" DEVICE is an electrode array that stimulates the tongue in a pattern based on the light intensity picked up by a camera.

Although sensory substitution techniques cannot fully restore sight, they do provide the information necessary for spatial orientation. Wicab had planned to submit BrainPort to the U.S. Food and Drug Administration for approval at the end of August, says Robert Beckman, president and chief executive officer of the company. He notes that the device could be approved for market by the end of 2009 for about $10,000 a machine.

Going with Golgi

Scientists create an artificial organelle for the first time

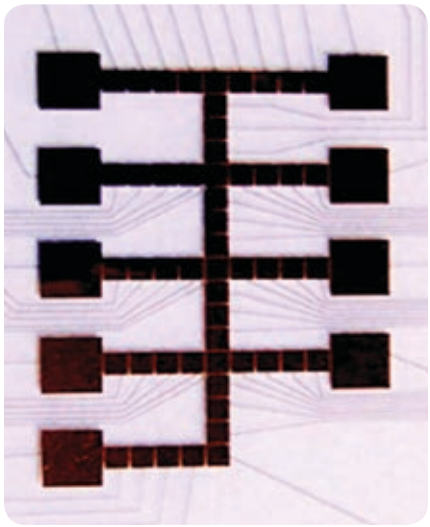
BY CHARLES Q. CHOI

In recent years scientists have made synthetic versions of key parts of the cell, such as chromosomes and ribosomes. Now researchers have developed the first working artificial prototype of an "organ" of a human cell—the Golgi apparatus.

Made up of a network of sacs piled together like a stack of pancakes, the Golgi apparatus chemically modifies proteins to help make them stable and functional, and it helps to manufacture complex sugars. But it remains one of the most poorly understood organelles. "The sacs are fluid and constantly change shape, so it's difficult to get a handle on," explains Robert Linhardt, a chemist at Rensselaer Polytechnic Institute. "And while we know the general direction of the flow of vesicles between stacks, we don't really know what cargoes they're carrying."

To better dissect how the Golgi apparatus works, Linhardt and his colleagues created a synthetic version of it, designing a square-millimeter-size lab-on-a-chip to mimic the assembly line of enzymes that modify a biomolecule within the Golgi apparatus. The sample molecules are attached to magnetic particles suspended in a watery droplet 300 billionths of a liter in size and placed on the chip. When the desired location on the chip for those molecules is electrically charged, it attracts the droplet and causes it to flow there. A larger magnet under that spot can keep in place the magnetic particles attached to the biomolecules. In this way, the drop can be moved through chambers loaded with an assembly line of enzymes, sugars and other raw materials.

In experiments with an inactive precursor of heparin, a widely used blood thinner, the scientists discovered their device could quickly and efficiently modify the anticoagulant to make it functional, findings they detail in the August 12 *Journal of the American Chemical Society*. The researchers suggest that an artificial Golgi could lead to a faster, safer method of producing heparin than current techniques, which employ animal tissue.



ARTIFICIAL GOLGI APPARATUS uses voltage to shuttle molecules among nine electrodes, where they are modified by enzymes.

Scientists have experimented with building up cells piece by piece for decades, including the creation of simple artificial cells in the form of bubbles made of synthetic cell membranes, to better understand how life on earth might have began. In 1997 researchers devised the first artificial human chromosome. And earlier this year molecular technologist George Church of Harvard University and his colleagues developed artificial ribosomes—bodies inside each cell that make proteins based on instructions from DNA—that functioned under cell-like conditions.

Linhardt and his co-workers plan on creating a synthetic endoplasmic reticulum (ER) as well, the organelle into which ribosomes are studded and where protein synthesis and folding take place. "We'd even like to integrate an artificial Golgi and ER together," Linhardt says. "We're basically taking pieces of a cell and making them on electronic chips," with the hope of moving to even more complex systems.

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

COURTESY OF WICAB ("*lollipop*" *device*); COURTESY OF ROBERT LINDHART *Rensselaer Polytechnic Institute (artificial Golgi)*

Hunting a Croc Killer

Mass deaths of South Africa's Nile crocodiles puzzle biologists BY NAOMI LUBICK

Carcasses of adult crocodiles do not usually signal the return of winter in South Africa, but mass death seems to be becoming the harbinger of the season. Rangers at the Kruger National Park have found Nile crocodiles floating in the Olifants River or bloated and decaying along its banks. Investigators are rushing to figure out the cause and worry that the deaths might be signaling the presence of toxins or pathogens that could threaten not only the croc population but also the livelihoods of the people living near the river.

The Olifants River runs several hundred kilometers through three South African provinces and into Mozambique. It supplies water to industrial agriculture operations that send food to Europe and to the local rural communities, which also depend on those waters for fishing and farming.

The first sign of croc trouble in the river came in the winter of 2008, when rangers collected 170 dead individuals, sometimes at a rate of 20 bodies a week. A survey at the end of this May showed nearly 400 crocs living in the park's gorge, down from at least 1,000 in 2008. So far, as of August 7, rangers and scientists have found 23 carcasses.

After slicing open some of the crocodile corpses last year, researchers determined some kind of pansteatitis—an inflammation of adipose tissue—was killing the animals. Specifically, their tails were swollen with the hardened, enlarged fat deposits, which had stiffened and immobilized the crocodiles and left them unable to hunt. Samples of the fat showed the deposits had oxidized to bright yellow.

The disease may not be limited to crocs. Scientists found the same kinds of fat deposits in fish in the Olifants River. And in the river's gorge just upstream from Massingir Dam in Mozambique, which also has seen croc declines, birds were absent, raising the possibility that they, too, have succumbed to the same agent.

But the cause behind the strange fattening remains a mystery. In June a team led by Henk Bouwman of North-West University, Potchefstroom Campus, in South Africa reported test results from crocodile tissues at two European chemistry meetings. "Everything is there," Bouwman says, referring to the detection of DDT, PCBs, dioxins and brominated flame retardants, "but nothing is screaming, 'it's me, it's me, it's me.' "

One possibility could be related to dinoflagellates and cyanobacteria found upstream in the catchment, which might be releasing toxins similar to those that cause red tides in marine environments, says Peter Ashton, a water resources specialist at the Council for Scientific and Industrial Research in South Africa and the University of Pretoria.

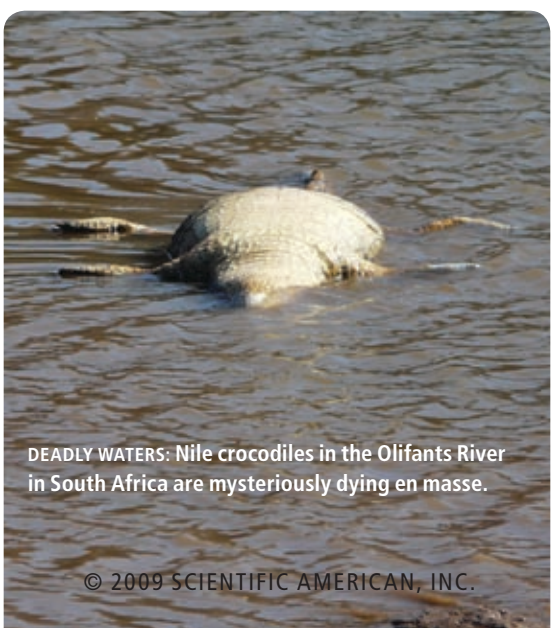
"It never is a quick, easy solution" in which it takes one test to find a culprit, explains Danny Govender, a disease ecologist for South African National Parks. She notes that samples taken from live crocs in 2007 showed that the fat of some crocodiles was beginning to harden. Along with Bouwman, she hypothesizes that all these toxins, found below harmful levels individually, could be acting together in a deadly brew.

Govender cites changes to the river's ecosystem that stem from infrastructure outside the park, including hundreds of coal-mining operations upstream, where crocodiles have disappeared almost completely, and a dam downstream of the gorge. For the first time in the two decades since it was built, the dam's reservoir was full last year, slowing down the Olifants's flow through the crocodiles' gorge. Govender wonders if the slowed water enabled toxins to build up along the crocodiles' stretch of the river. Indeed, hydrogen sulfide, ammonia and other compounds from river sediments probably caused massive fish deaths in July, scientists have concluded, and crocs eating these contaminated fish could have been affected.

Even if researchers find the culprits, the impacts could reach further than suspected. "We really underestimated [the number of dead] crocodiles from last year's count," Govender adds, noting that their bodies could have been eaten by other crocs or sunk to the bottom of the river. "I suspect we're losing a lot of breeding females," whose carcasses are smaller and more easily scavenged. If that is the case, she says, the gorge's crocodile population may not ever recover, even if scientists can pinpoint the cause of the die-off.

As for the people who depend on the Olifants River, "I don't know what to tell them," Bouwman says. His colleague Henrik Kylin of Swedish University of Agricultural Sciences in Uppsala wants to go into Mozambique to test fish there, and possibly people, to see if the croc killer kills more than just crocs.

Naomi Lubick is a freelance writer based in Folsom, Calif.



COURTESY OF HENK BOUWMAN

DEADLY WATERS: Nile crocodiles in the Olifants River in South Africa are mysteriously dying en masse.

Not Set in Stone (or Ice)

A new model for comet production revises the theory of their origins BY JOHN MATSON

The chunks of ice and dust that make their home in the Oort cloud, far beyond the orbit of Pluto, sometimes become dislodged and head into the solar system as streaky comets. Some disruptions, caused by passing stars and other interactions with the Milky Way galaxy, are severe enough to send Oort comets into orbits that buzz or even collide with Earth. New simulations have revealed a novel mechanism for their entry into our part of the solar system, a method that also suggests that comet showers may not have been strongly involved in major extinctions on Earth.

Comet dynamics depend heavily on Jupiter and Saturn: their huge gravitational fields tend to keep objects away from Earth. Comets that manage to skirt Jupiter and Saturn, the conventional thinking goes, had to have originated in the outer reaches of the Oort cloud, where perturbations from outside the solar system can be felt most strongly and are writ large across vast cometary orbits that take hundreds of years to complete. Only during comet showers caused by close stellar passages, the theory holds, have extreme gravitational disruptions brought inner Oort cloud comets into the mix.

A computer simulation by Nathan Kaib and Thomas Quinn, both at the University of Washington, have upended this thinking. They have found that the comets that manage to cross the Jupiter-Saturn barrier do in fact originate in large numbers in the inner Oort cloud, even in the absence of a large disruption causing a comet shower. Specifically, they found that the relatively nearby objects of the inner Oort cloud can be kicked into the reaches of the outer cloud via interactions with the massive planets. Those newly far-flung comets, suddenly enjoying a longer orbit and greater gravitational perturbations from interstellar space, can find their orbits so changed that, by the time they pass through the planetary region again, they slip past the gas giants. "They can basically hop over the Jupiter-Saturn barrier," Kaib says.

Kaib and Quinn estimate that more than half of the comets we observe streaking in from the Oort cloud reach our neighborhood via this route, and other researchers agree the simulation appears valid. "This mechanism, this dynamical path, as we call it, could work and could be a significant contributor," says Paul Weissman, a senior research scientist at the NASA Jet Propulsion Laboratory.

The new research presents a route for comet production "that goes some way" toward resolving discrepancies between the standard model and the observations, says Scott Tremaine, an astrophysicist at the Institute for Advanced Study in Princeton, N.J. "One of the issues is that [the conventional view of] the cometary formation process is so inefficient; in order to produce the number of comets that we see, you'd need a really massive protoplanetary disk, one that appears to be incompatible with our best estimates from other sources," Tremaine says.

Kaib and Quinn used their newfound mechanism, as well as the number of observed comets, to estimate an upper limit on how much material could be in the inner Oort cloud. They then produced a statistical model of how many comets would have hit Earth in comet showers in the past several hundred million years. Their conclusion: large cometary showers were few and hence probably did not cause more than one extinction event.

Using cometary dynamics to unwind the extinction history on Earth will likely meet with some controversy. Weissman notes that the extinction implications of Kaib and Quinn's analysis would involve comet showers, not comets in general, and that even a diminished profile of showers does not rule out the role of comets in extinctions. One big strike, rather than a shower of small ones, is all that's needed to trigger extinctions, he points out.

COMETARY COMMOTION: A new mechanism for how icy bodies get past Jupiter and Saturn suggests that comet showers did not play a big role in Earth's extinctions.

BETTMANN CORBIS

The Way the Wind Blows

The wind power industry requires stiff gusts. Global warming may not deliver

BY MICHAEL MOYER

THIS SUMMER SCIENTISTS PUBLISHED THE first study that comprehensively explored the effect of climate change on wind speeds in the U.S. The report was not encouraging. Three decades' worth of data seemed to point to a future where global warming lowers wind speeds enough to handicap the nascent wind industry. But the real story, like so much in climate science, is far more complex.

The study of decreased wind speeds came from a team led by Sara Pryor, professor and chair of the atmospheric science program at Indiana University. It examined wind speed data from hundreds of locations across the U.S. The team attempted to correct for any change in instrument position (such as what would happen if an airport places its anemometer atop a new control tower) and calculated for each site the average annual wind speed. Pryor and her colleagues found that in most of the U.S. wind speeds appear to be waning, in many locations by more than 1 percent a year.

The decline has the potential to be especially pernicious because turbines are exponentially sensitive to changes in wind speed. If the wind blows just 15 percent faster, a turbine will produce 50 percent more power. Conversely, a drop in average wind speed will significantly reduce the power output. Most of the locations that showed the most prominent decreases in wind speeds are strung along a corridor stretching from Texas to the Great Lakes that is home to 60 percent of the nation's installed wind power.

Yet the situation may not be as dire as the data imply. Direct observations of wind speeds are inherently problematic. Anemometers are far less accurate and consistent than thermometers, Pryor says. In addition, almost all the locations used in the study are close to fast-growing urban areas that can alter wind patterns in unpredictable ways. And unlike temperature measurements, which in some locations stretch back 150 years, relatively accurate and widespread wind measurements began only in the 1970s—hardly enough time to pluck a subtle trend out of noisy data.

DAVID MCNEW Getty Images

SENSITIVE SCALING: The amount of power a typical wind turbine produces increases exponentially with the speed of the wind.

Because direct measurements of wind speeds are so unruly, Pryor's team also tracked indirect measurements. These come from surface temperature and pressure records as well as balloon and satellite surveys. Computers crunch the data to produce a rich series of atmospheric portraits—a way to measure wind speeds without measuring the wind. This "reanalysis" data showed no change. Says Pryor: "If you have a mechanism causing your wind speeds to change"—global warming, for instance—"it should be evident in both the

observations and in the reanalysis data." If only one out of the two shows an effect, no one can say for sure what is going on.

For the wind industry, the most important change would be to peak wind speeds, because a turbine delivers most of its power only once the wind blows faster than about 25 miles per hour. Although the conclusions are preliminary, global climate models suggest that in the Northern Hemisphere, storm tracks should migrate northward, bringing more gusty storms to higher latitudes. "The northern part of the U.S. into Canada may see an increase" in peak wind speeds, Pryor says, "whereas the southern regions may see a decline."

Yet any decline should still leave wind farms with plenty to work with. A recent study by Xi Lu of Harvard University calculates that wind power in the U.S. could potentially generate 16 times the nation's current electricity production. The study limits potential wind farm locations to rural, nonforested sites (both on land and offshore) with high wind speeds. Worldwide, wind energy under the same constraints could supply at least 40 times the current electricity consumption.

According to Ryan Wiser, a staff scientist at Lawrence Berkeley National Laboratory and author of an upcoming special report on renewable energy and climate change by the Intergovernmental Panel on Climate Change, Lu's study simply confirms that "there is absolutely no resource constraint for wind in the U.S." Or, as Pryor puts it, "there may be regional winners and losers, but the winds are going to continue to blow."

Shifting Gears

To boost urban bicycling, figure out what women want BY LINDA BAKER

Getting people out of cars and onto bicycles, a much more sustainable form of transportation, has long vexed environmentally conscious city planners. Although bike lanes painted on streets and automobile-free "greenways" have increased ridership over the past few years, the share of people relying on bikes for transportation is still less than 2 percent, based on various studies. An emerging body of research suggests that a superior strategy to increase pedal pushing could be had by asking the perennial question: What do women want?

In the U.S., men's cycling trips surpass women's by at least 2:1. This ratio stands in marked contrast to cycling in European countries, where urban biking is a way of life and draws about as many women as men—sometimes more. In the Netherlands, where 27 percent of all trips are made by bike, 55 percent of all riders are women. In Germany 12 percent of all trips are on bikes, 49 percent of which are made by women.

"If you want to know if an urban environment supports cycling, you can forget about all the detailed 'bikeability indexes'—just measure the proportion of cyclists who are female," says Jan Garrard, a senior lecturer at Deakin University in Melbourne, Australia, and author of several studies on biking and gender differences.

Women are considered an "indicator species" for bike-friendly cities for several reasons. First, studies across disciplines as disparate as criminology and child rearing have shown that women are more averse to risk than men. In the cycling arena, that risk aversion translates into increased demand for safe bike infrastructure as a prerequisite for riding. Women also do most of the child care and household shopping, which means these bike routes need to be organized around practical urban destinations to make a difference.

MONICA BRADLEY

CYCLE TRACK, here along New York City's Ninth Avenue, keeps bicyclists physically separated from motor vehicle traffic. Such designs make riding safer and could boost the number of women cyclists.

"Despite our hope that gender roles don't exist, they still do," says Jennifer Dill, a transportation and planning researcher at Portland State University. Addressing women's concerns about safety and utility "will go a long way" toward increasing the number of people on two wheels, Dill explains.

So far few cities have taken on the challenge. In the U.S., most cycling facilities consist of on-street bike lanes, which require riding in vehicle-clogged traffic, notes John Pucher, a professor of urban planning at Rutgers University and longtime bike scholar. And

when cities do install traffic-protected off-street bike paths, they are almost always along rivers and parks rather than along routes leading "to the supermarket, the school, the day care center," Pucher says.

Although researchers have long examined the bike infrastructure in Europe, they have only just started to do so for the U.S. In a study conducted last year, Dill examined the effect of different types of bike facilities on cycling. The project, which used GPS positioning to record individual cycling trips in Portland, compared the shortest route with the path cyclists actually took to their destination. Women were less likely than men to try on-street bike lanes and more likely to go out of their way to use "bike boulevards," quiet residential streets with special traffic-calming features for bicycles. "Women diverted from the shortest routes more often," Dill says.

Other data support those findings. In New York City, men are three times as likely to be cyclists as women. Yet a bicycle count found that an off-street bike path in Central Park had 44 percent female riders. "Within the same city you find huge deviations in terms of gender," Pucher remarks.

Good infrastructure alone won't improve women's cycling rates, researchers caution. In an automobile-dominated culture, "attitudinal variables" also play a role, says Susan Handy, a professor of environmental science at the University of California, Davis. In a survey to be published in *Transportation Research Record,* Handy found that "comfort" and "needing a car" were important factors influencing women's cycling rates—but not men's. Needing a car is likely tied to the household errands women often perform, Handy says, and could be addressed in part by outreach programs showing that women can "jump on a bike the way they jump in a car."

A few municipalities are beginning to implement a "second wave" of strategies aimed at broadening the cycling demographic. In Portland, a city already renowned for its urban cycling, a Women on Bikes program targets such concerns as fixing a flat tire. The city is also building its first cycle track—a European-style bike lane that is separated from cars and pedestrians. Across the country state and federally funded Safe Routes to Schools programs are creating practical bike routes for kids so they don't have to be driven by their parents.

Ahead of the curve may be New York City, where about five miles of traffic-protected bike lanes have recently been installed. Credit goes to the new Department of Transportation commissioner Janette Sadik-Khan, who is upending the department's long-standing focus on trucks and automobiles. Remarks Pucher: "A woman cyclist became head of the DOT, and wonderful things started happening."

Linda Baker, based in Portland, Ore., likes to bike to the grocery store on low-traffic residential streets.

Too Little, Too Late

Long-standing liability issues leave us unprepared for a pandemic

BY THE EDITORS

As health care workers in the U.S. gear up for the flu season, they face a paradox: on the one hand, they will have too little vaccine against the novel influenza A (H1N1) strain to protect the entire population; on the other, some people will resist the shots that are offered to them. Sadly, both problems can be traced, at least in part, to the last time "swine flu" loomed. The 1976 national vaccination campaign against a pandemic that never materialized left the public with lingering doubts about whether the inoculations harmed some recipients and spawned lawsuits that cost the federal government nearly $100 million.

Since that episode, both public mistrust of vaccines and vaccine makers' mistrust of a litigious public have only grown—hampering the nation's ability to respond to the current, very real, pandemic. The Centers for Disease Control and Prevention expect the virus to sicken up to a third of the population this fall. But the nation will have barely enough vaccine for a third of its residents because methods used to make U.S. flu vaccines have changed little in half a century. Health officials decided early in the summer to stick with slow, egg-based production techniques and to eschew dose-sparing additives that might have tripled the vaccine supply.

In "Boosting Vaccine Power," beginning on page 72, Nathalie Garçon and Michel Goldman describe a new generation of adjuvants—immune-stimulating vaccine ingredients—that take advantage of scientific advances in understanding immune cell interactions. A few years ago the clinical trial of an experimental pandemic vaccine against bird flu containing one of these new adjuvants provided protection using less than a third of the usual amount of virus antigen in seasonal flu vaccines and produced minimal side effects. Another novel adjuvant has been approved for use in European seasonal flu vaccines for more than a decade.

Yet the U.S. does not permit use of the new adjuvants in vaccines, except in emergencies declared by the Food and Drug Administration (which is hardly likely to inspire public confidence). Even procuring a pandemic vaccine using traditional methods required the government to grant vaccine makers immunity from lawsuits and instead take the liability onto itself, as it did in 1976. Without such protections, vaccine makers were unwilling to enter the market. Fear of litigation had already driven most of them to leave the business. In the 1970s 25 companies made vaccines of all kinds. By 2004 only five remained.

In 2002 the SAFETY Act also granted immunity to potential makers of antibioterror vaccines and drugs. But the expedient of blanket immunity in an emergency is hardly a long-term solution to the crisis in vaccine development. In existing legislation, however, we have a model for a mechanism that would give reasonable compensation to victims of unforeseeable vaccine injuries while also shielding manufacturers from unpredictable legal liability for vaccines that work as intended. In 1986, recognizing the possibility that fundamental childhood vaccines could become unavailable if no one were willing to make them, Congress passed the National Childhood Vaccine Injury Compensation Act. It established a no-fault court to handle injury claims, with ceilings on potential damages. The settlements are financed by a tax on every vaccine dose. This system could be extended to all vaccines.

In 1985 an Institute of Medicine report, "Vaccine Supply and Innovation," advanced several other options for safeguarding vaccine research and thereby vaccine safety and supplies. Few viable alternatives have been offered since. It is impossible to know what vaccine technologies might have been available to meet the challenge of the influenza pandemic of 2009 had vaccine science not been bogged down by liability concerns for so long. But almost certainly one reason the U.S. has too little vaccine going into the fall is that attention to the decades-old issue of vaccine liability has been too late in coming. As policy makers tackle health care reform in the coming months, we call on them to address the problem of vaccine liability—both to restore public confidence in this critical health intervention and to ensure that the best and safest vaccine technologies are available before the next pandemic. ■

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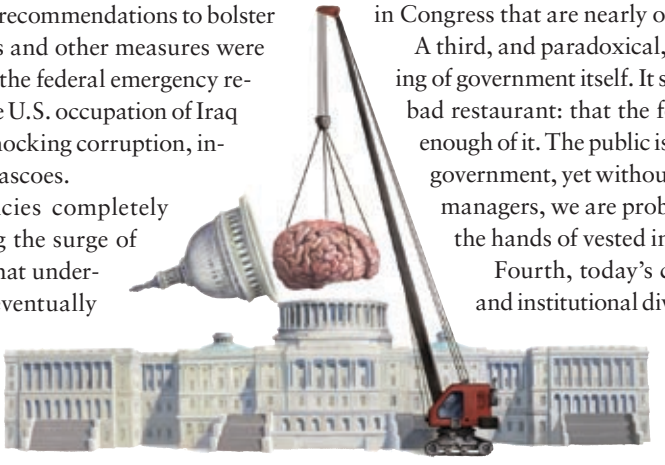
The Crisis of Public Management

Nothing less than an overhaul of the systems that implement federal policies will suffice

BY JEFFREY D. SACHS

The crisis of governance in the U.S. goes deeper than political divisions and ideology. It also extends to policy implementation. Not only are Americans divided on what to do about health care, budget deficits, financial markets, climate change and more, but government is also failing to execute settled policies effectively. Management systems linking government, business and civil society need urgent repair.

The systems failures are legion and notorious. The 9/11 attacks might have been prevented if the FBI and intelligence agencies had cooperated more effectively in early 2001 when they received signals of a possible terrorist attack. Hurricane Katrina caused mass devastation and loss of life because recommendations to bolster the levees protecting New Orleans and other measures were neglected for decades and because the federal emergency relief effort failed after the storm. The U.S. occupation of Iraq has been marked by massive and shocking corruption, incompetence and implementation fiascoes.



Government regulatory agencies completely dropped the ball while overseeing the surge of dangerous financial instruments that underpinned the reckless lending that eventually burst in the Great Crash of 2008. Military procurement systems are, according to some experts, so broken that they now jeopardize national security: the U.S. is buying overpriced, unneeded and technically defective armaments. Our costly federal health care system subsidizes the overuse of technologies while underfinancing highly effective and lower-cost public health measures. Despite nearly a decade of planning, the government has failed to build and test even a single coal-fired power plant that captures and sequesters its carbon dioxide, even though such a project is vital for a move to a low-carbon economy. The list, alas, goes on and on.

We need a better scientific understanding of these pervasive systems failures. Other nations' governments more successfully manage infrastructure investments, health systems and environmental resources, apparently with greater flexibility, less corruption, lower costs and better outcomes. America should be learning from their experiences.

Several factors are at play. One has been the flawed privatization of public-sector regulatory functions. Wall Street firms hold excessive sway over government regulators, so that dangerous behavior has been unconstrained. Private insurance companies and health care providers block measures to curtail the overuse of costly technologies. Private military suppliers drive the procurement of unneeded weapons systems.

A second has been the collapse of planning functions within the federal government. A remarkable feature of the recent debates over climate change, energy systems, infrastructure rehabilitation and health care reform is the lack of detailed forward-looking government proposals. The Obama administration has stated general principles (very admirable ones) but too often without clear targets and the operational strategies to achieve them. Planning has been replaced by lobbying and backroom deals in Congress that are nearly opaque to the public.

A third, and paradoxical, factor is the chronic underfunding of government itself. It sounds like the old joke about the bad restaurant: that the food was lousy and there wasn't enough of it. The public is wary of putting more funds into government, yet without investing more in skilled public managers, we are probably doomed to remain stuck in the hands of vested interests and lobbies.

Fourth, today's challenges cut across specialties and institutional divisions. In health care and energy, for example, the private sector holds the key technologies, but only the public sector can finance R&D, regulate sustainable practices, and ensure access for the poor to resources and services. Public health must be addressed through curative medical care, nutrition, food systems and a safer man-made environment. Energy systems must respect both ecological and economic constraints. Yet government agencies are not designed to take an integrated approach.

Tinkering will no longer suffice: we need an overhaul of basic public management systems to regain control over regulatory processes, reduce lobbying, restore planning, adequately fund skilled managers and align those management systems with holistic strategies. ■

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

SCI AM An extended version of this essay is available at **www.ScientificAmerican.com/oct2009**

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Captain Hook Meets Adam Smith

Debunking pirate myths reveals how hidden economic forces generate social order

BY MICHAEL SHERMER

Will Turner: "If we can outrun her, we can take her. We should turn and fight."
Captain Jack Sparrow: "Why fight when you can negotiate?"
—*Pirates of the Caribbean: Dead Man's Chest*

From countless films and books we all know that, historically, pirates were criminally insane, traitorous thieves, torturers and terrorists. Anarchy was the rule, and the rule of law was nonexistent.

Not so, dissents George Mason University economist Peter T. Leeson in his myth-busting book, *The Invisible Hook* (Princeton University Press, 2009), which shows how the unseen hand of economic exchange produces social cohesion even among pirates. Piratical mythology can't be true, in fact, because no community of people could possibly be successful at anything for any length of time if their society were utterly anarchistic. Thus, Leeson says, pirate life was "orderly and honest" and had to be to meet buccaneers' economic goal of turning a profit. "To cooperate for mutual gain—indeed, to advance their criminal organization at all—pirates needed to prevent their outlaw society from degenerating into bedlam." There is honor among thieves, as Adam Smith noted in *The Theory of Moral Sentiments:* "Society cannot subsist among those who are at all times ready to hurt and injure one another.... If there is any society among robbers and murderers, they must at least ... abstain from robbing and murdering one another."

Pirate societies, in fact, provide evidence for Smith's theory that economies are the result of bottom-up spontaneous self-organized order that naturally arises from social interactions, as opposed to top-down bureaucratic design. Just as historians have demonstrated that the "Wild West" of 19th-century America was a relatively ordered society in which ranchers, farmers and miners concocted their own rules and institutions for conflict resolution way before the long arm of federal law reached them, Leeson shows how pirate communities democratically elected their captains and constructed constitutions. Those documents commonly outlined rules about drinking, smoking, gambling, sex (no boys or women allowed onboard), use of fire and candles, fighting and disorderly conduct, desertion and shirking one's duties during battle. (The last could lead to the "free rider" problem in which the even division of loot among uneven efforts leads to resentment, retaliation and economic chaos.) Enforcement was key. Just as civil courts required witnesses to swear on the Bible, pirate crews had to consent to the captain's codes before sailing. In the words of one observer: "All swore to 'em, upon a Hatchet for want of a Bible. When ever any enter on board of these Ships voluntarily, they are obliged to sign all their Articles of Agreement ... to prevent Disputes and Ranglings afterwards." Thus, the pirate code "emerged from piratical interactions and information sharing, not from a pirate king who centrally designed and imposed a common code on all current and future sea bandits."

From where, then, did the myth of piratical lawlessness and anarchy arise? From the pirates themselves, who helped to perpetrate the myth to minimize losses and maximize profits. Consider the Jolly Roger flag that displayed the skull and crossbones. Leeson says it was a signal to merchant ships that they were about to be boarded by a marauding horde of heartless heathens; the nonviolent surrender of all booty was therefore perceived as preferable to fighting back. Of course, to maintain that reputation, pirates occasionally had to engage in violence, reports of which they provided to newspaper editors, who duly published them in gory and exaggerated detail. But as 18th-century English pirate Captain Sam Bellamy explained, "I scorn to do any one a Mischief, when it is not for my Advantage." Leeson concludes, "By signaling pirates' identity to potential targets, the Jolly Roger prevented bloody battle that would needlessly injure or kill not only pirates, but also innocent merchant seamen."

This economic analysis also explains why Somali pirates typically receive ransom payoffs instead of violent resistance from shipping crews and their owners. It is in everyone's economic interest to negotiate the transactions as quickly and peacefully as possible. Markets operating in a lawless society are more like black markets than free markets, and because the Somali government has lost control of its society, Somali pirates are essentially free to take the law into their own hands. Until Somalia establishes a rule of law and a lawful free market for its citizens, lawless black market piracy will remain profitable. Until then, an-*arrgh*-chy will reign. ■

Michael Shermer is publisher of Skeptic *magazine (www.skeptic.com) and author of* The Mind of the Market.

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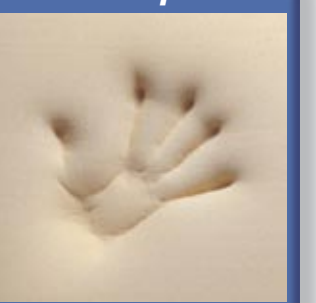

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Space, the Final Frontier?

Let's stop kidding ourselves about why we really want to go back to the moon

BY LAWRENCE M. KRAUSS

This year marked the 40th anniversary of two momentous events related to space exploration. One, the *Apollo 11* moon landing on July 20, 1969, was a hallmark technological achievement. The other, the complete first run of Stanley Kubrick's remarkable movie *2001: A Space Odyssey,* vividly depicted author Arthur C. Clarke's vision of humans traveling the solar system with abandon.

Much of the related flurry of reporting noted the stark differences between reality—people have not been back to the lunar surface since the December 1972 visit—and Clarke's idea. Articles also asked whether the nation is sufficiently committed to devoting the $200 billion or so to returning to the moon 10 years from now and perhaps, after that, spending even more money to send humans to Mars.

As a 15-year-old, I found the 1969 moon landing enthralling. I also charted the entire Apollo missions, built scale models and dreamed of being the first Canadian astronaut. Humankind's travels promised to propel science forward. But since then, my perception of the proper role for human space exploration has changed.

I would still jump at the chance to go into space. But I now recognize, as I testified to Congress almost a decade ago (coincidentally along with Buzz Aldrin, from *Apollo 11*), that doing so would be for the adventure, not for advancing science. The most scientifically exciting knowledge we can gain about the universe and the solar system will involve unmanned space vehicles, robotic devices and a lot less money than lofting Americans beyond Earth's orbit.

Human spaceflight has proved inordinately costly and far more dangerous than the Apollo program's successes led us to believe. Moreover, the associated difficulties are far more mundane than TV and movie science fiction suggest. We are not held back for lack of a warp drive, although fuel costs are a reason why unmanned flights are so much cheaper; missions that carry humans must drag along the paraphernalia required to keep them alive. The chief obstacle to visiting Mars is cosmic radiation. During the 18 months or so that a round-trip journey would take, astronauts would very likely receive a lethal dose of radiation.

Our ultimate destiny may be in the stars, but the limitations imposed by physics and our biology suggest that this future probably is to be reserved for our mechanical progeny—robots—or perhaps for computers that can get organic life rebooted on some distant locale.

In the near term we still crave adventure, and the desire to travel to, and perhaps to colonize, the moon and maybe Mars seems irresistible, if financially daunting. I am not against sending humans into space for that reason (and would also encourage consideration of one-way missions, which seem to be ultimately more fiscally practical). But we should separate funding for science from the diversion of a costly manned space program. We also should not waste huge amounts on boondoggles such as the $100-billion International Space Station, which purported to offer useful science beyond mere experience with how humans can live 200 miles above Earth's surface for extended periods.

The Apollo program taught us that we may conquer even enormous technological problems if the nation is willing to focus for however long it takes to solve them and to devote tremendous resources. We now face many such challenges, from climate change to energy independence, which we need to tackle even as we juggle our hunger for space travel.

I do not believe that this is a zero-sum game. Maybe there is money to do it all: to send humans into space, to do the best fundamental science we can do and also to address pressing problems here on Earth. But we can only do that if we are honest about the costs, and possible benefits, of science for humanity. And we must not pretend that a base on the moon or Mars is a panacea for any of our significant problems back home. ■

Lawrence M. Krauss, a theoretical physicist, commentator and book author, is Foundation Professor and director of the Origins Initiative at Arizona State University (http://krauss.faculty.asu.edu).

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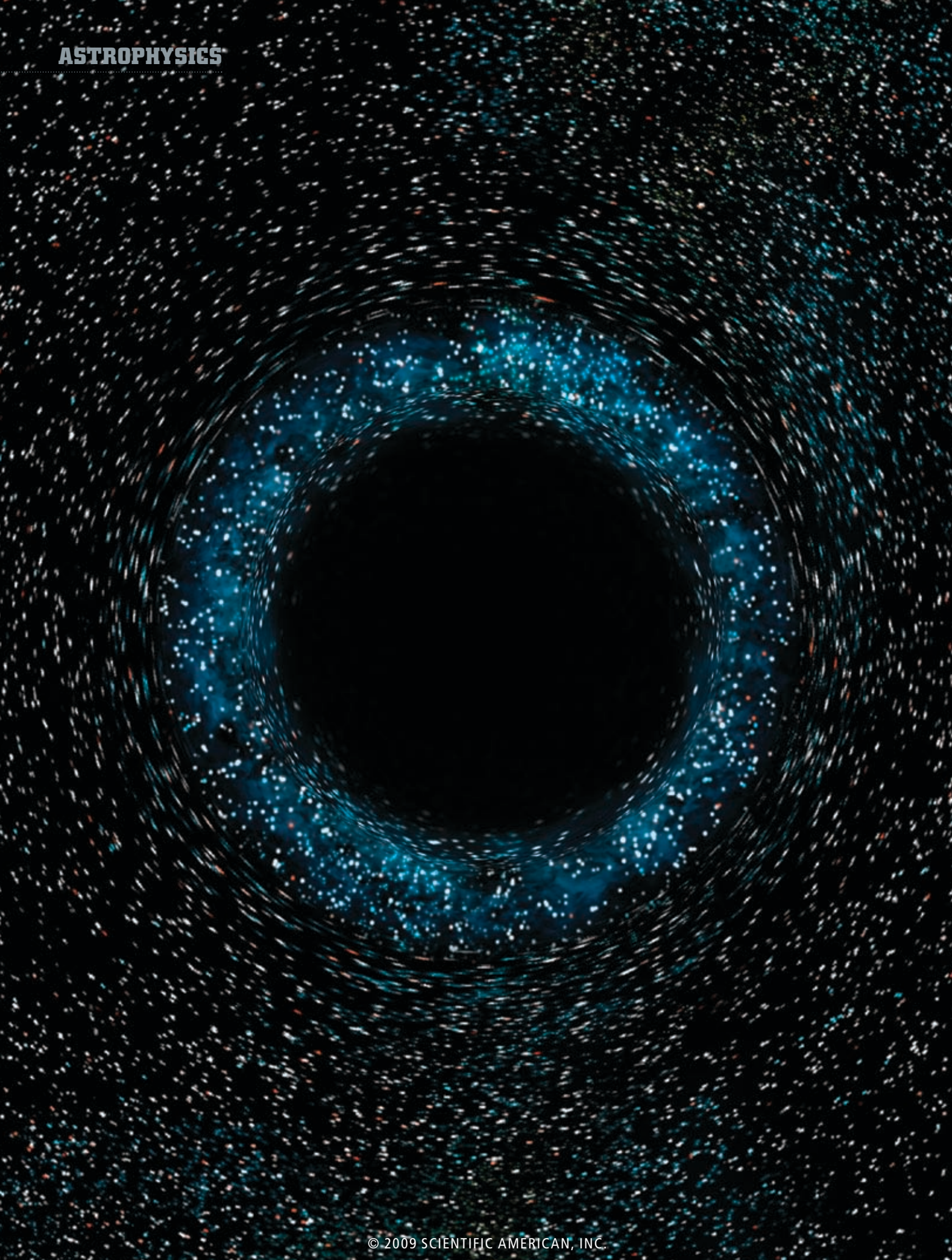
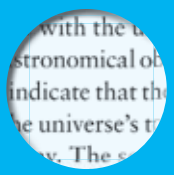


BLACK STARS, NOT HOLES



Quantum effects may prevent true black holes from forming and give rise instead to dense entities called black stars

BY CARLOS BARCELÓ, STEFANO LIBERATI, SEBASTIANO SONEGO AND MATT VISSER

Black holes have been a part of popular culture for decades now, most recently playing a central role in the plot of this year's *Star Trek* movie. No wonder. These dark remnants of collapsed stars seem almost designed to play on some of our primal fears: a black hole harbors unfathomable mystery behind the curtain that is its "event horizon," admits of no escape for anyone or anything that falls within, and irretrievably destroys all it ingests.

To theoretical physicists, black holes are a class of solutions of the Einstein field equations, which are at the heart of his theory of general relativity. The theory describes how all matter and energy distort spacetime as if it were made of elastic and how the resulting curvature of spacetime controls the motion of the matter and energy, producing the force we know as gravity. These equations unambiguously predict that there can be regions of spacetime from which no signal can reach distant observers. These regions—black holes—consist of a location where matter densities approach infinity (a "singularity") surrounded by an empty zone of extreme gravitation from which nothing, not even light, can escape. A conceptual boundary, the event horizon, separates the zone of intense gravitation from the rest of spacetime. In the simplest case, the event horizon is a sphere—just six kilometers in diameter for a black hole of the sun's mass.

So much for fiction and theory. What about reality? A wide variety of high-quality astrophysical observations indicates that the universe does contain some extremely compact bodies that emit essentially no light or other radiation of their own. Although these dark objects have masses ranging from just a few suns to well over a million suns, their diameters, as best astrophysicists can determine, range from only several kilometers to millions of kilometers—matching general relativity's predictions for black holes of those masses.

Yet are these dark and compact bodies that astronomers observe really the black holes predicted by general relativity? The observations to date certainly fit the theory quite well, but the theory itself is not entirely satisfactory in the way that it describes black holes. In particular, general relativity's prediction that a singularity resides inside every black hole suggests that the theory fails at that location, as is usually the case when a theory predicts that some quantity is infinite. Presumably general relativity fails by not

KEY CONCEPTS

- Black holes are theoretical structures in spacetime predicted by the theory of general relativity. Nothing can escape a black hole's gravity after passing inside its event horizon.
- Approximate quantum calculations predict that black holes slowly evaporate, albeit in a paradoxical way. Physicists are still seeking a full, consistent quantum theory of gravity to describe black holes.
- Contrary to physicists' conventional wisdom, a quantum effect called vacuum polarization may grow large enough to stop a hole forming and create a "black star" instead.

—The Editors

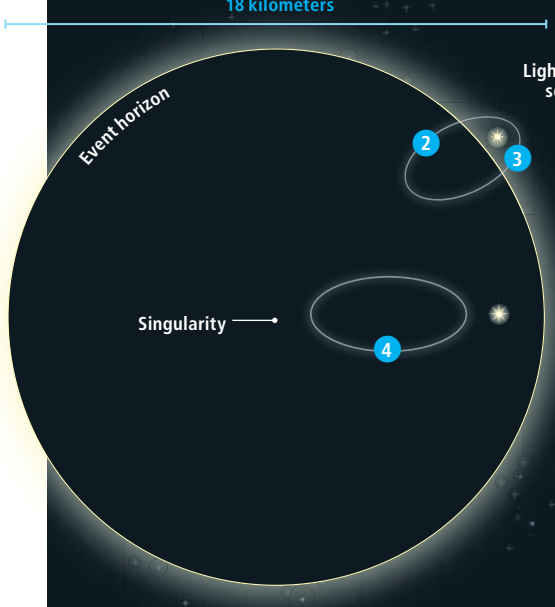
EUROPEAN SPACE AGENCY, NASA AND FELIX MIRABEL
French Atomic Energy Commission, Institute for Astronomy and Space Physics/Conicet of Argentina

[BASICS]

BLACK HOLES IN BRIEF

A black hole is a region of curved spacetime with such intense gravity that nothing can escape. Its defining feature is its event horizon: the boundary of the region of no escape. A black hole is mostly empty, its mass apparently collapsed to a location with infinite density—a "singularity"—deep inside the horizon.

A black hole with three times the mass of the sun would have a diameter of about 18 kilometers, comparable to the length of Manhattan.



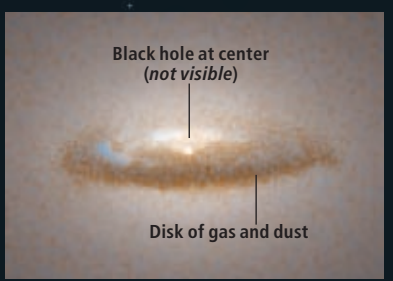
Far away from large masses, a flash of light spreads out symmetrically in all directions 1.

Just outside a black hole's event horizon, the gravity captures most of a flash 2.

Some light escapes, just 3.

If a flash occurs anywhere inside an event horizon, all the light is drawn into the black hole's singularity 4.

▶ In practice, black holes can be observed via the material orbiting and falling into them. The image at the right, taken in 1998 by the Hubble Space Telescope, shows a vast disk of gas and dust believed to have a supermassive black hole at its center. Strictly speaking, however, such observations inform scientists only that an extremely compact, heavy object emitting little or no light of its own is present; they do not provide absolute proof that the object is a black hole.



LUCY READING-IKKANDA (*illustration*); NASA, ROELAND P. VAN DER MAREL *Space Telescope Institute* AND FRANK C. VAN DEN BOSCH *University of Washington* (*dust disk around black hole*)

taking into account quantum effects, which matter and energy exhibit at the microscopic scale. The search for a modified theory that incorporates quantum mechanics, generically called quantum gravity, is a powerful engine driving a lot of activity in theoretical physics research.

This need for a quantum theory of gravity raises fascinating questions: What would quantum-corrected black holes be like? Would they be radically different from classical black holes, or would their classical description remain a good approximation? The four of us have shown that certain quantum effects may well prevent black holes from forming at all. Instead a kind of object we have named a black star could arise. A black star would be blocked from taking the final plunge to infinite density and from becoming enveloped in an event horizon. The black star would be supported by something not normally considered to be a sturdy construction material: space itself.

The Weight of Quantum Nothingness

We derive our conclusions by applying a venerable approach known as semiclassical gravity, but without making all the same assumptions about the collapsing matter that previous studies have made—to see if we might avoid the paradoxical territory arrived at by those studies. In the absence of a full-fledged theory of quantum gravity, theorists have resorted to semiclassical gravity over the past 30-odd years to analyze how quantum mechanics alters black holes. This method partially incorporates aspects of quantum physics—in particular, quantum field theory—into classical Einsteinian gravity.

Quantum field theory describes each kind of fundamental particle—the electron, the photon, quarks, you name it—in terms of a field that fills space, much like the electromagnetic field. Quantum field theory's equations are usually set up in flat spacetime, that is, in the absence of gravity. Semiclassical gravity uses quantum field theory as formulated in curved spacetime.

In the broadest terms, the strategy of semiclassical gravity goes as follows: a collection of matter in some configuration would, according to classical general relativity, produce some specific curved spacetime. Yet the curvature of spacetime modifies the energy of the quantum fields. This modified energy, according to classical general relativity, changes spacetime's curvature. And so on, iteration after iteration.

The goal is to obtain a self-consistent solution—a curved spacetime containing a configuration of quantum fields whose energy generates that same curvature. That kind of self-consistent solution ought to be a good approximation to how reality behaves in many situations involving quantum effects and gravity even though gravity itself has not been described by a quantum theory. Semiclassical gravity thus incorporates quantum corrections into general relativity in a "minimal" way, taking into account the quantum behavior of matter but still treating gravity (that is, spacetime curvature) classically.

This approach, however, immediately runs into an embarrassing problem in that the straightforward calculation of the quantum fields' lowest possible (or "zero point") energy—the energy when no particles of any kind are present, the en-

ergy of the vacuum—produces an infinite result. This problem actually comes up already with ordinary quantum field theory (that is, in flat space, no gravity). Fortunately for theorists wishing to predict particle physics phenomena that do not involve gravity, the particles behave in ways that depend on only the energy differences between states, so the value of the quantum vacuum energy plays no role. Careful subtraction schemes known as renormalization take care of the infinities, allowing the energy differences to be computed with extremely high precision.

With gravity in the picture, however, the vacuum energy matters. An infinite energy density would seem to produce an extremely large curvature of spacetime—that is, even "empty" space would harbor an intense gravitational force, which is not remotely compatible with the universe that we actually observe. Astronomical observations over the past decade indicate that the net zero-point contribution to the universe's total energy density is extremely tiny. The semiclassical gravity approach does not attempt to solve this problem. Instead it is customary to assume that *whatever* the solution is, it exactly cancels the zero-point contribution to the energy density in flat spacetime. This assumption makes for a consistent semiclassical vacuum: the energy density is zero everywhere, for which general relativity predicts flat spacetime.

If some matter is present, spacetime is curved, which alters the quantum fields' zero-point energy density, which means the zero-point energy is no longer exactly canceled. The excess amount is said to be caused by vacuum polarization, by analogy with the effect of an electric charge polarizing a medium [*see box on next page*].

We have described these features of semiclassical gravity in terms of mass and energy density, but in general relativity it is not only those quantities that produce spacetime curvature. The momentum density and the pressures and stresses associated with a specific gravitating substance also do so. A single mathematical-physics object, known as the stress energy tensor (SET), describes all these curvature-producing quantities. Semiclassical gravity assumes that the quantum fields' zero-point contributions to the total SET are exactly canceled in flat spacetime. The mathematical-physics object obtained applying such a subtraction procedure to the SET is called the renormalized stress energy tensor (RSET).

BLACK HOLE CATEGORIES

General relativity predicts that a black hole is completely defined by just three quantities: mass, angular momentum and electric charge. It makes no difference what went into the hole—matter, antimatter or energy, or all three combined.

Astronomers have observed holes in three mass classes: Holes of about five to 15 solar masses are formed from dying stars. Many galaxies harbor a hole of millions to billions of solar masses at their core. Holes of a few thousand solar masses have been detected in the center of globular star clusters.

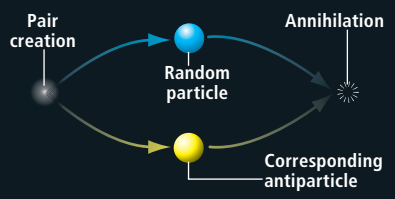
[PARADOX]

THE TROUBLE WITH QUANTUM BLACK HOLES

The classical (that is, nonquantum) equations of general relativity forbid anything emerging from inside a black hole's event horizon. Yet in the 1970s Stephen W. Hawking carried out quantum calculations that predicted black holes would randomly emit particles at a very low rate (*left panel*). The randomness created a paradoxical scenario (*right panel*) known as the information problem.

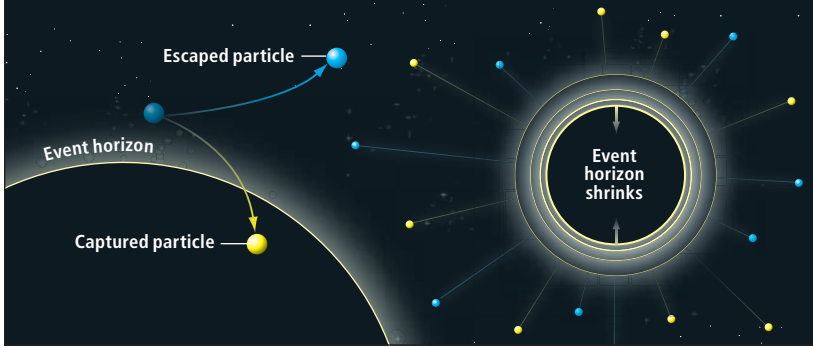
HAWKING RADIATION IS EMITTED

Even in empty space, a quantum process constantly produces pairs of so-called virtual particles and antiparticles, which immediately annihilate each other.



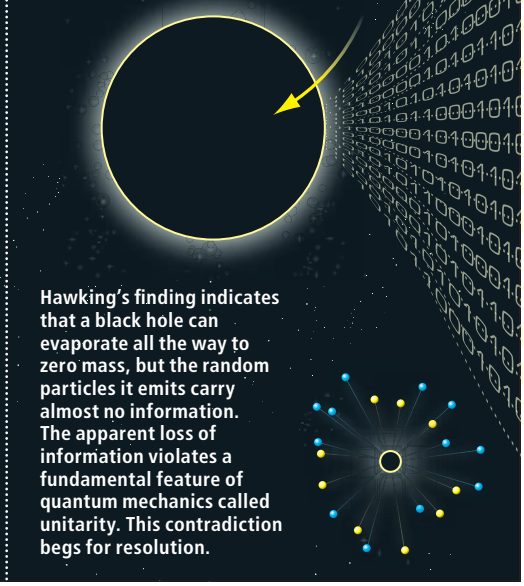
Near a black hole's event horizon, one virtual particle may be captured by the black hole, and the second may escape. The escaped particle carries away positive mass, and the captured one takes negative mass into the black hole—thereby reducing the hole's mass.

Thus, if nothing falls into the black hole, its mass and its event horizon gradually shrink. This evaporation process speeds up as the hole becomes smaller.



INFORMATION IS LOST

Matter that falls into a black hole carries with it a vast quantity of information.



Hawking's finding indicates that a black hole can evaporate all the way to zero mass, but the random particles it emits carry almost no information. The apparent loss of information violates a fundamental feature of quantum mechanics called unitarity. This contradiction begs for resolution.

LUCY READING-IKKANDA

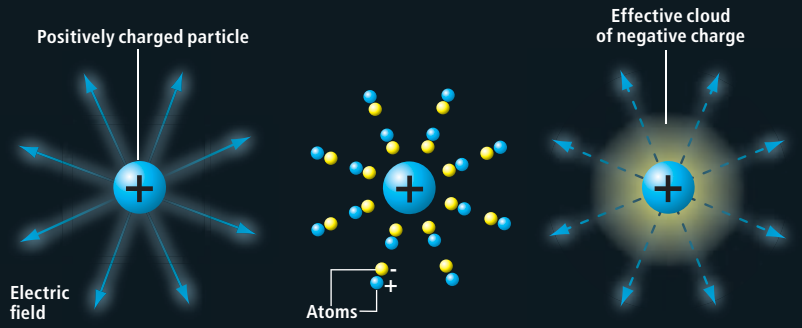
[QUANTUM PRIMER]

WHAT EMPTINESS CAN DO

In classical general relativity, spacetime is dynamic, its curvature producing gravity. A quantum effect known as vacuum polarization provides another way that empty space can play an active role in the universe.

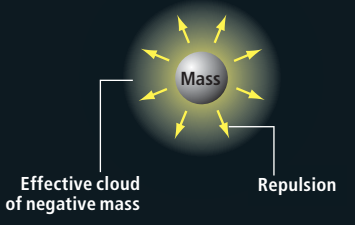
ELECTRIC ANALOGY

In a medium, a charged object's electric field (*left*) polarizes nearby atoms (*center*), reducing the total electric field (*right*). Quantum field theory reveals that even a vacuum can be polarized, because an electric field polarizes virtual particle/antiparticle pairs.



VACUUM POLARIZATION

In general relativity, the role of electric charge is played by mass and energy and that of the electric field by curved spacetime, or gravity. The vacuum polarization produces an energy deficit (in effect a cloud of negative energy) and a repulsive force.



When applied in curved spacetime, the subtraction scheme still succeeds in canceling the SET's divergent part but leaves a finite, nonzero value for the RSET. The end result is the following iterative process: classical matter curves spacetime via Einstein's equations, by an amount determined by the matter's classical SET. This curvature makes the quantum vacuum acquire a finite nonzero RSET. This vacuum RSET becomes an additional source of gravity, modifying the curvature. The new curvature induces in turn a different vacuum RSET, and so on.

Quantum-Corrected Black Holes

With the approach of semiclassical gravity spelled out, the question becomes: How do these quantum corrections affect predictions about black holes? In particular, how do the corrections alter the process of forming a black hole?

The simplest black hole of some mass (say, M times the solar mass) is one that is not rotating and not electrically charged. Such a hole has a radius R that works out to be $3M$ kilometers. The radius R is called the gravitational radius or Schwarzschild radius for that mass. If for any reason some matter has collapsed to occupy a region smaller than its gravitational radius, it has formed a black hole; it has disappeared inside its own event horizon.

The sun, for instance, has a 700,000-kilometer radius, which is much larger than its gravitational radius (three kilometers). The relevant semiclassical gravity equations make it clear that the RSET of the quantum vacuum in this situation is negligible. Thus, the sun is far from forming a black hole according to the classical equations, and quantum corrections do not alter this picture. Indeed, astrophysicists can safely ignore quantum gravity effects when analyzing the sun and most other astronomical objects.

The quantum corrections can become significant, however, if a star is not much larger than its gravitational radius. In 1976 David G. Boulware, now at the University of Washington, analyzed the case of such a compact star when the star is stationary (that is, not collapsing). He showed that the closer the star is to its gravitational radius, the larger the vacuum RSET near its surface becomes, increasing to infinite energy density. This result implies that semiclassical gravity theory does not permit a stationary black hole (meaning one whose event horizon remains constant in size) as a solution of its equations.

Boulware's result, however, does not tell us what to expect in the case of a star undergoing a collapse that would lead to a black hole according to classical general relativity. Stephen W. Hawking had already tackled this situation a year earlier, using somewhat different techniques, to show that a classical black hole formed by collapse emits random particles. More precisely, the particles have a distribution of energies characteristic of thermal radiation; the black hole has a temperature. He conjectured that quantum-corrected black holes would be essentially classical black holes subject to slow evaporation via this radiation. A black hole of one solar mass has a temperature of 60 nanokelvins. The corre-

[THE AUTHORS]

Carlos Barceló, Stefano Liberati, Sebastiano Sonego and Matt Visser have been collaborating in various combinations and permutations since the new millennium. Barceló is professor of theoretical physics and a vice director at the Institute of Astrophysics of Andalusia in Spain. Liberati is assistant professor of astrophysics at the International School for Advanced Studies in Trieste, Italy. Sonego is professor of mathematical physics at the University of Udine in Italy. Visser is professor of mathematics at Victoria University of Wellington in New Zealand.

LUCY READING-IKKANDA

sponding evaporation rate is so slow that absorption of cosmic background radiation would completely overwhelm the evaporation and the hole would grow in size. An evaporating black hole of such a mass would be indistinguishable from a classical black hole in practice because the evaporation would be immeasurably small.

Considerable effort by theorists in the decade after Hawking's paper, including the approximate calculation of the RSET in collapsing configurations, reinforced this picture as being the correct one. Today the standard view in the physics community is that black holes form as described by classical general relativity and subsequently undergo slow quantum evaporation via Hawking radiation.

Quantum matter always seems to find new ways of delaying gravitational collapse.

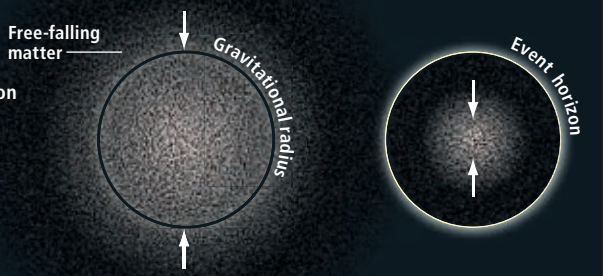
[THE AUTHORS' PROPOSAL]

A BLACK STAR IS BORN

A black hole forms when some matter collapses under its own weight and no force can stop it. Physicists' conventional wisdom is that quantum effects cannot be large enough to stop such a collapse. The authors disagree.

FAST COLLAPSE IS NOT HALTED

The vacuum polarization is negligible for free-falling matter, even when the matter gets dense enough to form an event horizon and become a black hole.

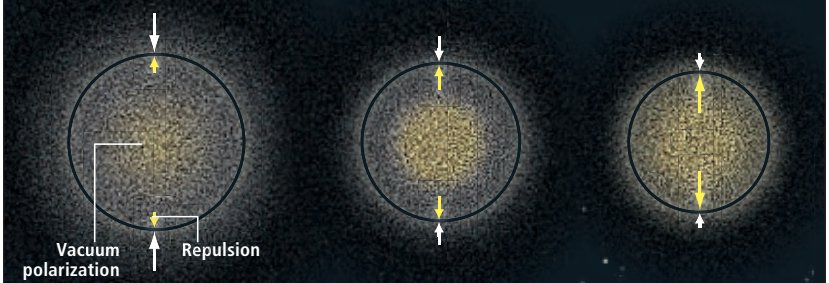


SLOWER COLLAPSES MAY BE DELAYED FOREVER

If the matter's fall is slowed, vacuum polarization may grow, producing repulsion.

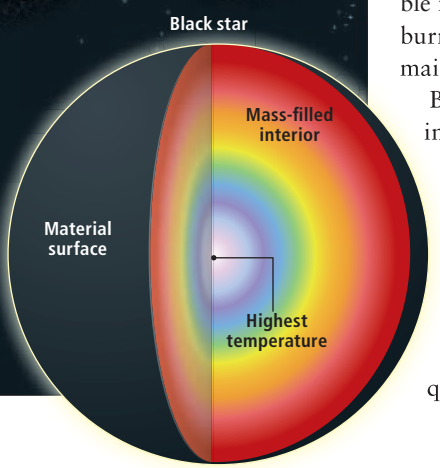
The repulsion further slows the collapse, which allows the polarization to intensify.

The collapse is delayed from ever forming an event horizon.



BLACK STAR

The result is a black star. The gravitational field around it is identical to that around a black hole, but the star's interior is full of matter and no event horizon forms. A black star could emit Hawking-like radiation, but this radiation carries the information that went into the black star, preserving unitarity. If a black star could be peeled layer by layer like an onion, at each stage the remaining core would be a smaller black star, also emitting radiation. Small black holes emit more radiation and have higher temperatures than larger ones, and so a black star is increasingly hot toward its center.



LUCY READING-IKKANDA

The Information Problem

Hawking's discovery of black hole evaporation, along with earlier results by Jacob D. Bekenstein of the Hebrew University of Jerusalem uncovered a deep—and as yet not fully understood—relation among gravity, quantum physics and thermodynamics. At the same time, it opened up new problems. Perhaps the most important is known as the information problem, which is closely related to the question of the final outcome of black hole evaporation.

Take the example of a large star undergoing gravitational collapse. The star embodies a vast amount of information in the positions and velocities and other properties of its more than 10^{55} particles. Suppose the star forms a black hole but then, gradually over the aeons, evaporates by emitting Hawking radiation. A black hole's temperature is inversely proportional to its mass, and thus an evaporating black hole becomes hotter and evaporates faster as its mass and radius shrink. A huge explosion ejects the last of the black hole's mass. But what remains afterward? Does the hole completely vanish, or does some kind of small remnant remain? In either case, what has happened to all the information of the star? According to Hawking's calculation, the particles radiated by the hole carry essentially no information about the star's initial state. Even if some kind of black hole remnant remains, how could such a small object contain all the information that was in the original star?

The disappearance of information matters because one of the most fundamental pillars of quantum theory is that quantum states evolve in a manner that is called unitary, one consequence of which is that no information ought to ever be truly obliterated. Information may be inaccessible in practice, such as when an encyclopedia burns up, but in principle the information remains in the swirling smoke and ashes.

Because the calculations that predict Hawking radiation rely on semiclassical gravity, physicists cannot be sure if information loss is an artifact of the approximations involved or a feature that will remain when we discover how to compute the process exactly. If the evaporation process does destroy information, the correct full quantum gravity equations must violate the unitary nature of quantum mechanics as we know it. Conversely

ly, if information is preserved and a complete theory of quantum gravity will reveal where it is in the radiation, either general relativity or quantum mechanics seems to need modification.

A Radically Different Alternative

The information problem and related puzzles have motivated us (and others) to revisit the line of reasoning that led physicists in the 1970s to the picture of evaporating almost classical black holes. We have found that the old semiclassical prediction that black holes form from gravitational collapse even when quantum effects are considered depends on several technical and often unstated assumptions.

In particular, the old calculations assume that collapse proceeds very rapidly, taking about the same time as would be needed for material at the star's surface to free-fall to the star's center. We found that for a slower collapse, quantum effects may produce a new kind of very compact object that does not have an event horizon and is thus much less problematic.

As we have already mentioned, the RSET of the quantum vacuum in a spacetime curved by a typical star is negligible everywhere. When the star starts to collapse, the RSET might change. Nevertheless, the old conclusion that the RSET remains negligible continues to hold if the collapse is about as fast as free falling.

Yet if the collapse proceeds significantly slower than free falling, the RSET can acquire arbitrarily large and negative values in the region near the Schwarzschild radius—where the classical event horizon would have formed. A negative RSET produces a repulsion, which further slows the collapse. The collapse might come to a complete halt just short of forming a horizon, or it might continue forever at an ever slower pace, becoming ever closer to forming a horizon but never actually producing one.

This result, however, does not make it impossible for black holes to form. A perfectly homogeneous spherical cloud of matter of, say, 100 million solar masses falling freely under its own weight would surely produce an event horizon. Such a large cloud would have a density comparable to that of water when it became compact enough to form a horizon. At such a low density the RSET cannot become large enough to prevent the horizon from forming. But we know that what happened in the universe did not follow this script. The vast, nearly homogeneous clouds of matter that emerged from the early stages of the big bang did not collapse to form black holes. Instead a sequence of structures developed.

First, stars formed, the heat of their nuclear reactions delaying the collapse for a long time. When a star largely exhausts its nuclear fuel, it may develop into a white dwarf or, if massive enough, explode as a supernova, leaving behind a neutron star (a sphere made of neutrons that is only somewhat larger than the star's gravitational radius). In either case,

[ALTERNATIVE BODIES]

OTHER WAYS OUT OF A HOLE

Many researchers have proposed more or less exotic objects that could serve as alternatives to the conventional (but apparently paradoxical) idea of an evaporating black hole and account for the dark, compact bodies observed by astronomers. The common feature of these proposals (and our own black star hypothesis) is that the new object would lack an event horizon.

GRAVASTARS

The spacetime geometry around a "*grav*itational *vac*uum *star*" would be indistinguishable from that of a black hole down to about 10^{-35} meter away from the spherical region where the classical black hole horizon would have been located. The horizon would be replaced by a shell of matter and energy a mere 10^{-35} meter thick (known as the Planck length—the length scale at which quantum gravity effects are expected to become large). The gravastar's interior would be empty space with a large vacuum polarization, which would produce a repulsion that prevents the matter shell from collapsing any further. In a variant of the gravastar proposal, the classical notions of geometry break down in the region separating the interior and exterior.

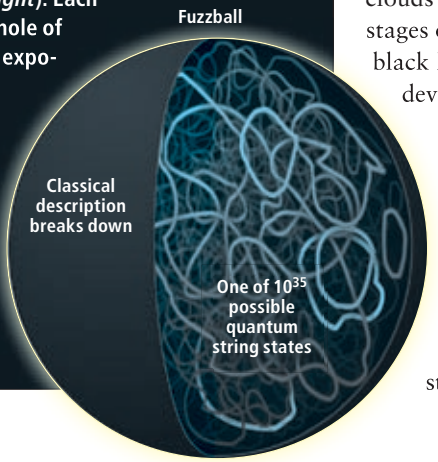
BLACK HOLE COMPLEMENTARITY

In conventional quantum mechanics, complementarity refers to the idea that an observation may reveal either the particle nature of an object or the wave nature, but not both. Similarly, the quantum mechanics of black holes might embody a new kind of complementarity. An observer who remains outside a black hole may have one description of the observable geometry (for instance, imagining a membrane having certain physical properties in place of the event horizon), whereas an observer who falls into the hole must use a different description.

FUZZBALLS

Proponents of "fuzzballs" contend that the horizon would be a transition region between the exterior classical geometry and a quantum interior where no definite notion of spacetime could be specified. The interior would be describable by string theory and would not have a singularity (*right*). Each exterior geometry (say, the geometry of a black hole of exactly 10^{30} kilograms) could have any one of an exponentially large number of such stringy quantum states as its interior. The semiclassical view of a black hole—with an event horizon, an enormous entropy, a temperature and emission of thermal Hawking radiation—would amount to a statistical average over all the possible interiors, analogous to a description of a volume of gas that disregards the exact positions and motions of the individual atoms.

—C.B., S.L., S.S. and M.V.



LUCY READING-IKKANDA

it is actually a purely quantum effect—the Pauli exclusion principle—that prevents further collapse. The neutrons in the neutron star cannot enter the same quantum state, and the resulting pressure resists the gravitational collapse. A similar story for ions and electrons explains why a white dwarf is stable.

If the neutron star acquires more mass, eventually the crushing gravitational load overwhelms the neutrons, and further collapse occurs. We do not know for certain what happens next (although the conventional view says a black hole forms). Scientists have suggested a variety of objects that might form—such as so-called quark stars, strange stars, boson stars and Q-balls—that would be stable at pressures too great for a neutron star. Physicists must develop a better understanding of how matter behaves at densities well beyond that of neutrons to know which conjecture, if any of them, is correct.

Thus, experience tells us that matter following the laws of quantum mechanics always seems to find new ways of delaying gravitational collapse. Although any of these roadblocks may be overcome (a typical stable configuration can always be made unstable by adding enough matter), each process that delays collapse provides additional time for the quantum vacuum's negative RSET to pile up and become significant. This RSET could take over the task of counterbalancing the gravitational pull, and because its repulsion may increase without limit, it can stop the matter's collapse to a black hole forever.

Black Stars

The resulting bodies would be the new kind of object we have named black stars. Because of their extremely small size and high density, they would share many observable properties with black holes, but conceptually they would be radically different. They would be material bodies, with a material surface and an interior filled with dense matter. They would be extremely dim because light emitted from their surface would be very redshifted—the light wave greatly stretched—in traveling from the intensely curved space near the black star to distant astronomers. In principle, astronomers could conduct complete astrophysical studies of black stars because no event horizon would present an obstacle.

Within the family of bodies of black star type, some might resemble evaporating black holes by emitting radiation similar to Hawking radiation. For the specific case in which collapse approaches formation of a horizon but never quite stops, we have shown that a black star could emit particles with a so-called Planckian energy spectrum (which is very similar to a thermal spectrum), at a temperature very slightly smaller than the Hawking temperature. By having no horizon, the black star cannot lock away any information. Instead the emitted particles and whatever matter remains behind with the black star carry all the information. Standard quantum physics would describe the formation and evaporation process. Black stars do not completely solve the information problem, however, as long as ways remain for event horizons to form somewhere in the universe.

These evaporating objects could be called quasi black holes because when viewed from the outside they would have approximately the same thermodynamic properties as evaporating black holes. Their interiors, however, would harbor a rainbow of temperatures, rising to a maximum near the center. If you imagine the body as an onionlike structure of concentric shells, each shell would be slowly shrinking, never quite compact enough for the combined mass of the shell and everything inside it to form a horizon. Each shell would be prevented from collapsing by the vacuum RSET that we predict will develop where the conditions for a horizon are approached slowly enough. The deeper shells would have higher temperatures, just like smaller-mass black holes do. We do not yet know whether these appealing objects show up naturally or whether they are exceptional.

Over the Horizon

Study of black holes has always provoked a great variety of reactions from researchers. On the one hand, it is exciting to think that they hide within them the door to unforeseeable new possibilities in physics, albeit only for those who dare to enter. On the other hand, implications of black holes have long disturbed some physicists—the quest for alternatives to black holes, often motivated by distaste for one or another of their features, is as old as the idea of black holes themselves.

Our black star proposal and other researchers' black hole alternatives all have the common theme that the spacetime around them is essentially identical to that around a classical black hole, down to extremely close to where the horizon would have formed. Although the secret door leading to an understanding of how quantum physics merges with gravity remains out of our sight, it may not be shielded from us by the impenetrable fortress of an event horizon. ■

WHAT'S NEXT

Future work on the black star scenario must show specific physical systems for which vacuum polarization succeeds in halting a collapse according to semiclassical gravity.

By describing quantum black holes as bundles of fundamental entities called branes, string theorists have reproduced predictions of semiclassical gravity for certain special cases. They hope to extend these results to all kinds of black holes.

A definitive resolution of the information problem and of the fate of collapsing matter will most likely require development of a complete quantum theory of gravity.

MORE TO EXPLORE

Fate of Gravitational Collapse in Semiclassical Gravity. Carlos Barceló, Stefano Liberati, Sebastiano Sonego and Matt Visser in *Physical Review D,* Vol. 77, No. 4; February 19, 2008.

Small, Dark, and Heavy: But Is It a Black Hole? Matt Visser, Carlos Barceló, Stefano Liberati and Sebastiano Sonego in *Proceedings of Black Holes in General Relativity and String Theory*; August 2008. Available at **http://arxiv.org/abs/0902.0346**

The Fuzzball Proposal for Black Holes. K. Skenderis and M. Taylor in *Physics Reports,* Vol. 467, No. 4–5, pages 117–171; October 2008. **http://arxiv.org/abs/0804.0552**

The Black Hole War: My Battle with Stephen Hawking to Make the World Safe for Quantum Mechanics. Leonard Susskind. Little Brown, 2008.

TURBOCHARGING THE BRAIN

Will a pill at breakfast improve concentration and memory—and will it do so without long-term detriment to your health?

By Gary Stix

The symbol H+ is the code sign used by some futurists to denote an enhanced version of humanity. The plus version of the human race would deploy a mix of advanced technologies, including stem cells, robotics, cognition-enhancing drugs, and the like, to overcome basic mental and physical limitations.

The notion of enhancing mental functions by gulping down a pill that improves attention, memory and planning—the very foundations of cognition—is no longer just a fantasy shared by futurists. The 1990s, proclaimed the decade of the brain by President George H. W. Bush, has been followed by what might be labeled "the decade of the better brain."

Obsession with cognitive enhancers is evidenced in news articles hailing the arrival of what are variously called smart drugs, neuroenhancers, nootropics or even "Viagra for the brain." From this perspective, an era of enhancement has already arrived. College students routinely borrow a few pills from a friend's Ritalin prescription to pull an all-nighter. Software programmers on deadline or executives trying to

SPLASHLIGHT

maintain a mental edge gobble down modafinil, a newer generation of pick-me-ups. Devotees swear that the drugs do more than induce the wakefulness of a caramel macchiato, providing instead the laserlike focus needed to absorb the nuances of organic chemistry or explain the esoterica of collateralized debt obligations.

An era of enhancement may also be advanced by scientists and drugmakers laboring to translate research on the molecular basis of cognition into pharmaceuticals meant specifically to improve mental performance—mainly for people suffering from dementias. But a drug that works for Alzheimer's or Parkinson's patients might inevitably be prescribed by physicians far more broadly in an aging population with milder impairments. Widely publicized debates over the ethics of enhancement have reinforced the sense that pills able to improve cognition will one day be available to us all.

Academic and news articles have asked whether cognitive enhancers already give some students an unfair advantage when taking college entrance exams or whether employers would step over the line if they required ingestion of these chemicals to meet a company's production deadlines.

But even as articles are published on the "boss turns pusher," doubts have arisen about the reality of drugs for strengthening brainpower. Do current drugs developed for attention problems or excessive sleepiness really allow a student to do better on an exam or an executive to perform flawlessly under sharp questioning from a board of directors? Will any drug that fiddles with basic brain functions ever be safe enough to be placed on pharmacy shelves alongside nonprescription pain relievers and antacids? All these questions are now provoking heated deliberations among neuroscientists, physicians and ethicists.

Ethical Dissonance

Arguments about safety, fairness and coercion aside, demand is indeed high for cognitive enhancers that are otherwise prescribed for conditions such as ADHD. Based on government data gathered in 2007, more than 1.6 million people in the U.S. had used prescription stimulants nonmedically during the previous 12 months. Legal

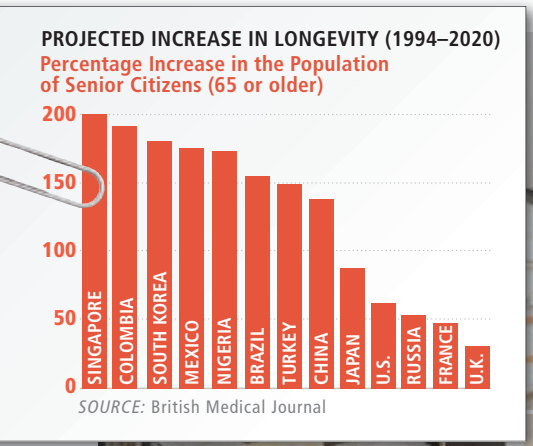
KEY CONCEPTS

- College students and executives ingest stimulant drugs to enhance routine mental performance, although the compounds were never approved for that purpose.
- Some ethicists and neuroscientists have raised the prospect of making these drugs widely available for enhancement of healthy people who do not suffer from dementia.
- Questions remain about whether any drug that tinkers with basic mental functioning will be sufficiently safe and effective to be consumed like coffee or tea.

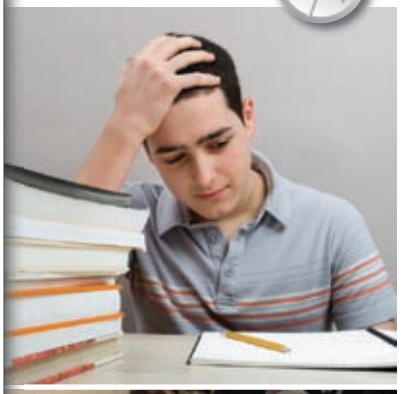
—The Editors

Why Enhance?

An aging population (*graph*), ubiquitous Internet pharmacies, and a workforce and student population strapped with deadlines and performance pressures (*photographs*) help to explain the fascination with cognitive-enhancing drugs.



SOURCE: British Medical Journal



One ethicist has proposed a plan in which Ritalin could end up alongside Pepto-Bismol on drugstore shelves.

medicines in this category include methylphenidate (Ritalin), the amphetamine Adderall, and modafinil (Provigil). On some campuses, one quarter of students have reported using the drugs. And an informal online reader survey by *Nature* last year showed 20 percent of 1,427 respondents from 60 countries polled about their own use said they had used either methylphenidate, modafinil or beta blockers (the last for stage fright). Overall, a need for improved concentration was the reason cited most frequently. People often manage to acquire the drugs on the Internet or from doctors, who can prescribe medicines approved for one purpose to treat something else (drugmakers, however, cannot legally promote such "off label" uses).

Ingestion of these chemicals will likely grow along with an aging population and an increasingly globalized economy. "If you're a 65-year-old living in Boston and your retirement savings have decreased dramatically and you have to stay on the job market and compete with a 23-year-old in Mumbai to stay alert and stay effective, you may feel pressured to turn to these compounds," says Zack Lynch, executive director of the Neurotechnology Industry Organization.

The recent push for ethical guidelines, of course, presumes that these drugs are better than placebos and do in fact improve some aspect of cognition, be it attention, memory or "executive function" (planning and abstract reasoning, for instance). Given that assumption, many argue, it behooves ethicists to consider the ramifications of the popularity of these drugs. Such logic led in 2002 to a new academic discipline, neuroethics, meant in part to address the moral and social questions raised by cognition-enhancing drugs and devices (brain implants and the like).

Taking a highly provocative stand, a group of ethicists and neuroscientists published a commentary in *Nature* last year raising the prospect of a shift away from the notion of drugs as a treatment primarily for illness. The article suggested the possibility of making psychostimulants widely available to the able-minded to improve performance in the classroom or the boardroom, provided the drugs are judged to be safe and effective enough for healthy people. Citing research demonstrating the benefits of these drugs on memory and various forms of mental processing, the investigators equated pharmaceutical enhancement with "education, good health habits, and information technology—ways that our uniquely innovative species tries to improve itself."

Six months later one of the article's authors, John Harris, a bioethicist at the University of Manchester in England, went further in an opinion piece in the *British Medical Journal*. Harris, editor of the *Journal of Medical Ethics* and a book called *Enhancing Evolution,* noted that if methylphenidate is judged safe enough to be used in children, it should be considered sufficiently innocuous for consumption by adults interested in turbocharging their brains. In a later interview, Harris said he foresaw a gradual loosening of restrictions, and if no safety problems arise, the drug (a controlled substance in the U.S.) could ultimately become an over-the-counter purchase, like aspirin.

These musings have not gone unchallenged. Other researchers and ethicists have questioned whether drugs that modulate mental processes will ever have a safety profile that will justify their being dispensed in the same fashion as

LUCY READING-IKKANDA (*graph and pills*); GETTY IMAGES (*man studying*); LARRY DALE GORDON (*man in office*)

a nonprescription painkiller or coffee or tea.

"People say that cognitive enhancement is just like improving vision by wearing glasses," says James Swanson, a researcher at the University of California, Irvine, who was involved with clinical trials for both Adderall and modafinil for ADHD. "I don't think people understand the risks that occur when you have a large number of people accessing these drugs. Some small percentage will likely become addicted, and some people may actually see mental performance decline. That's the reason I'm opposed to their general use." Along these lines, the British Home Office, the interior ministry, is awaiting a report from an advisory panel on whether the potential harm from nonmedical use of enhancers requires new regulations.

Other scientists assert that the debate may be moot because improving smarts might not be possible through any means but the tedious exercise of cramming for a calculus exam. Some who have tried to develop drugs to reverse the memory loss of dementia doubt whether enhancement of the healthy is anything but a remote possibility. "I would not worry much about implications of cognitive enhancers in the healthy, because there are no cognitive enhancers to worry about," says Rusiko Bourtchouladze, author of a popular book about the science of memory and a researcher who contributed to the work that led to a Nobel Prize for Eric R. Kandel in 2000. "To talk about cognitive enhancement, it's too, too early, and these drugs may not arrive even in our lifetime. There's too much noise about this."

In this view, the complex mix of chemical signals, enzymes and proteins that collaborate to form a memory creates a self-regulating balance that resists tinkering unless disrupted by disease. The decline in thought processes and sense of identity that comes with dementia might be addressable by compensating for losses of key chemicals and might merit the risk of untoward side effects from drug intervention. But upsetting the fragile stasis in the healthy could produce unintended consequences: as just one example, any improvement in long-term memory (the place where recollections of childhood and last year's vacation reside) could be countered by diminished capacity for working memory (the mental scratch pad where your brain stores a telephone number temporarily).

Some critics of those who argue over the ethics of neuroenhancement attribute the current flap to what they call "speculative ethics." This tendency also besets nanotechnology and other technological endeavors in which ethicists, scientists and policy makers are diverted by discussions of the social implications of technologies yet to be invented, be they smart pills or nanorobots run amok. "A significant part of the debate on human enhancement … suffers from inflated expectations and technology hype," notes Maartje Schermer of Erasmus University Rotterdam and her colleagues in the journal *Neuroethics*.

A Checkered History

The notion that existing drugs might enhance cognition in the healthy dates back for the better part of a century and has produced ambiguous results. Chemist Gordon Alles introduced amphetamine for medical use in 1929, a synthetic drug chemically similar to the Chinese herb ephedrine. (Alles also devised the drug Ecstasy, another amphetamine.) Various forms were dispensed on both sides during World War II to keep soldiers awake and alert and to bolster courage. The Germans and Japanese ingested methamphetamine, while the British and Americans used Benzedrine, a similar drug to Adderall.

[ON PHARMACY SHELVES]

BRAIN BOOSTERS. REALLY?

The scientific literature and popular press commonly cite the medicines below—approved for neurological disorders—as having potential to improve mental functioning in unimpaired people. The evidence is decidedly mixed, however, and even if the drugs do prove helpful, their risks may keep the agents from gaining approval by regulators for marketing to healthy individuals.

DRUG	MEDICAL USE	EFFECTIVENESS AS ENHANCER	RISKS
Methylphenidate (Ritalin, Concerta and others) and **amphetamines** (Adderall and others)	Stimulants used for treatment of attention-deficit hyperactivity disorder (ADHD) and narcolepsy (uncontrollable sleep spells)	Increase cognitive performance on certain tasks under conditions of fatigue; may improve planning and one type of working memory; appear to increase functioning on dull, repetitive tasks	Could worsen performance in a subset of users or on complex tasks; cardiovascular complications and seizures, hallucinations and addiction
Modafinil (Provigil)	Newer-generation stimulant for narcolepsy and excessive sleepiness because of shift work or obstructive sleep apnea	Appear to augment mental focus and better performance on a limited set of cognitive measures, such as recall of long strings of numbers	May have a higher potential for addiction than originally thought; may cause serious skin rashes
Donepezil (Aricept)	Treatment for the cognitive deficits of Alzheimer's disease; increases the neurotransmitter acetylcholine to improve cognition	Might aid in learning or memory, but overall results are equivocal; may take several weeks to work and is not as widely used off-label as the drugs above	Could cause a slight deterioration in cognitive performance in healthy individuals

LUCY READING-IKKANDA (*pills*)

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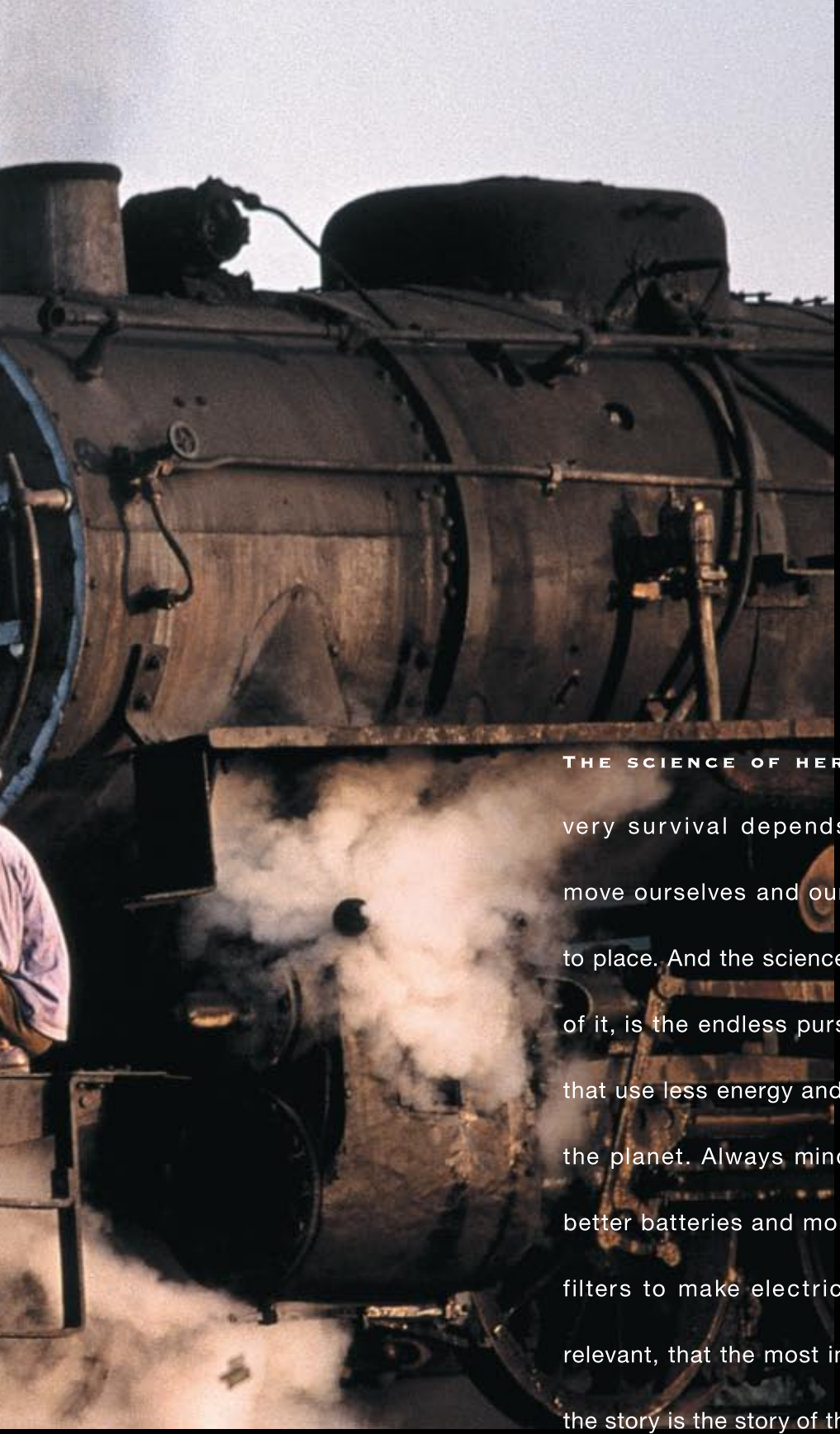

THE SCIENCE OF HERE TO THERE. Our very survival depends on our ability to move ourselves and our needs from place to place. And the science of it, the chemistry of it, is the endless pursuit of ways to do it that use less energy and are less harmful to the planet. Always mindful, as we develop better batteries and more effective filters to make electric and diesel power relevant, that the most important element of the story is the story of the elements. Carbon. Hydrogen. Oxygen. And human.

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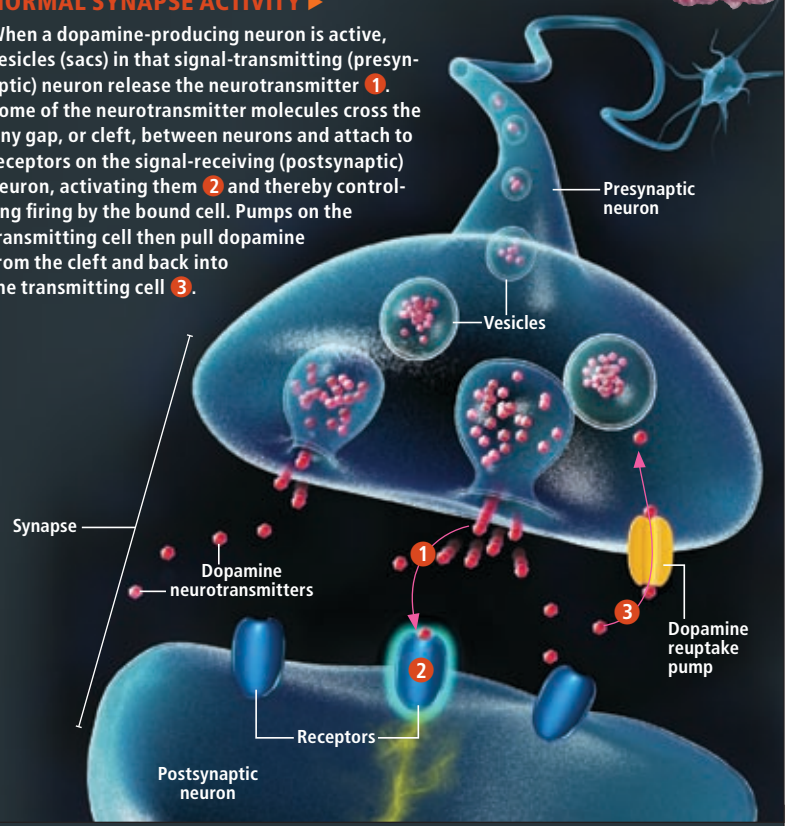
[MECHANISMS]

HOW TWO ENHANCERS WORK

Some purported enhancers, such as methylphenidate and amphetamines, alter the activity of the neurotransmitter dopamine in the synapses, the junction between neurons. Enhanced dopamine signaling may improve learning by focusing attention and interest on a task.

NORMAL SYNAPSE ACTIVITY ▶

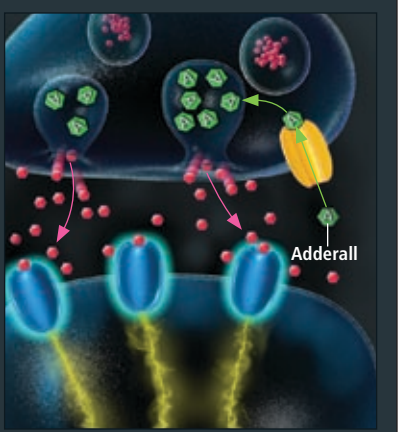
When a dopamine-producing neuron is active, vesicles (sacs) in that signal-transmitting (presynaptic) neuron release the neurotransmitter 1. Some of the neurotransmitter molecules cross the tiny gap, or cleft, between neurons and attach to receptors on the signal-receiving (postsynaptic) neuron, activating them 2 and thereby controlling firing by the bound cell. Pumps on the transmitting cell then pull dopamine from the cleft and back into the transmitting cell 3.



▼ DRUG-ENHANCED SYNAPSE ACTIVITY

Methylphenidate (Ritalin and Concerta, for instance) blocks the reuptake of dopamine. More dopamine is available to attach to a postsynaptic neuron, which amplifies the strength of the signal transmitted from the presynaptic neuron.

Adderall and other amphetamines enter the presynaptic neuron through the pumping mechanism and cause dopamine to be displaced into the synaptic cleft, increasing the amount of neurotransmitter available to act on the postsynaptic cell.



Scientists soon wanted to know whether the perceived benefit in performance was genuine. Psychological assessments by both British and Americans during the 1940s found that users self-rated their performance highly on tests that measured reading speed, multiplication and other factors. But their test scores, in most tasks, were no better than those earned by subjects who ingested caffeine. Performance, in fact, could decline on more complex tasks. "Because of their mood-elevating effects, amphetamines tend to make us feel we are performing especially well, when in fact we are not," says Nicolas Rasmussen, a historian of science at University of New South Wales in Sydney and author of the book *On Speed* (New York University Press, 2008). "In simplistic lab tests assessing performance on boring tasks, they boost scores by increasing diligence, but that's not the same as taking a law school exam or flying in combat."

Methylphenidate, a close chemical relative of the amphetamines, emerged in 1956 as a supposedly milder and gentler form of stimulant ("the happy medium in psychomotor stimulation," in the words of the drugmaker), but both its biochemical and psychological effects are similar when adjusted for dose. The halcyon era for amphetamines occurred nearly 40 years ago. U.S. consumption reached as much as 10 billion pills in the late 1960s before the Food and Drug Administration clamped down and labeled them as controlled substances that required a special prescription. Neuroscientist Michael S. Gazzaniga of the University of California, Santa Barbara, one of the authors of the *Nature* commentary, remembers his father sending him Benzedrine for studying when he was in college in the early 1960s.

In the mid-1990s the growing use of methylphenidate for treatment of ADHD prompted researchers to deploy novel brain-imaging techniques and sophisticated neuropsychological tests to examine effects of the drug in healthy subjects, supplying a baseline for comparison with patients with ADHD and other neuropsychiatric disorders. A 1997 paper in *Psychopharmacology* by Barbara Sahakian, Trevor Robbins and their colleagues at the University of Cambridge showed that methylphenidate improved cognitive performance on several measures (spatial working memory and planning, in particular) in a group of rested, healthy young males but not on others, including attention and verbal fluency. As testing progressed, the volunteers seemed to make more errors in their responses,

ANDREW SWIFT

perhaps because of impulsivity induced by effects of the drug.

The same researchers found little cognitive benefit in healthy elderly males. And in 2005 a group at the University of Florida Medical School at Gainesville could not turn up any cognitive boost from the drug among 20 sleep-deprived medical students. Another impediment to methylphenidate ever being placed alongside NoDoz and other caffeine pills is its potential for causing cardiac arrhythmias and for abuse as a recreational drug. Addiction is rare with normal dosing. But in the 1970s methylphenidate users routinely became addicted after inhaling or injecting the drug that they called "West Coast."

The Always-On Drug

The checkered legacy of amphetamines prompted neuroscientists and physicians to hail the arrival of modafinil as a wakefulness-promoting agent with a seemingly more favorable side effect and abuse profile than the amphetamines. The ability of modafinil (introduced in the U.S. in 1998) to allow people to work long stretches without the need for breaks has turned it into a lifestyle drug for the jet-lagged who attempt to live in four time zones at once.

Jamais Cascio, an associate of the Institute for the Future in Palo Alto, Calif., obtained a prescription for modafinil from his physician after hearing about it from friends who traveled a lot. On trips overseas, he noticed that it made him feel not only more awake but also sharper. "The perceived increased cognitive focus and clarity was very much of a surprise, but it was a very pleasant surprise," says Cascio, who has mentioned the drug in some articles he has written. "My experience was not that I'd become a superbrain. It was more an experience of more easily slipping into a state of cognitive flow, a state of being able to work without distraction."

Testing has confirmed some of Cascio's impressions. In 2003 Sahakian and Robbins found that 60 rested, healthy male volunteers did better on a few neuropsychological measures, such as recall of numerical sequences, but results were unchanged on others. Investigators elsewhere have also found benefits for the drug, although, as Cascio noted, it will not make a dunce into a genius. None of these studies, moreover, has tested effects on cognition over extended periods.

Unregulated availability of either modafinil or methylphenidate also remains unlikely because the drugs tend to affect individuals in different ways. Users with lower IQs appear to derive a large performance boost from modafinil, whereas those with more innate ability show little or no benefit. With methylphenidate, those having poor working memory improved when tested; those having a naturally higher memory capacity showed much smaller benefits.

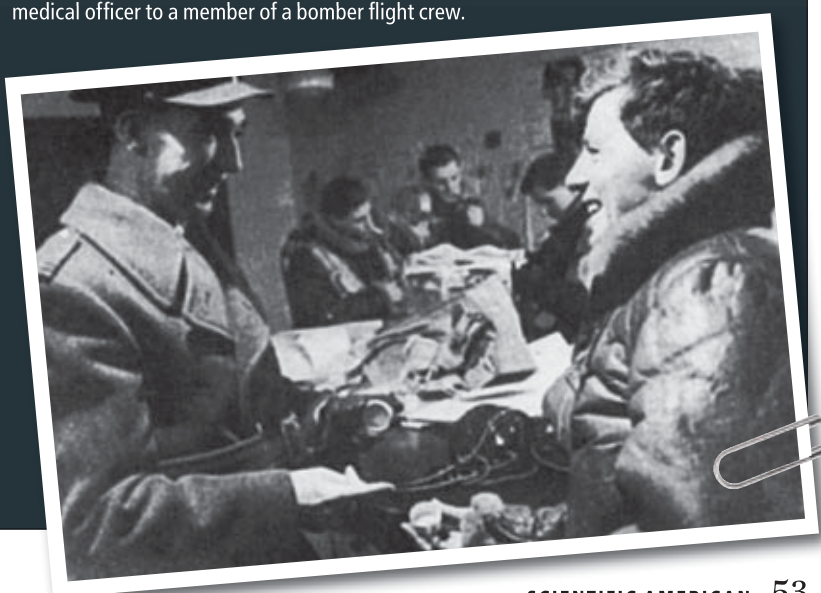
As with amphetamines, modafinil did not emerge from a basic understanding of the underlying biology of how the brain works. Present research shows, however, that the drug seems to involve multiple neurotransmitters, the chemicals that trigger the firing of specific clusters of neurons. The drug's exact mechanism remains to be elucidated. But recently Nora D. Volkow, director of the National Institute on Drug Abuse, and her colleagues discovered that one of those neurotransmitters is dopamine, the same chemical that is boosted by amphetamines and that imbues those drugs with their addiction potential. "It appears that methylphenidate and modafinil are very similar in what they're doing to the dopamine system in the brain, contrary to what was believed," says Volkow, although she adds that it is not practical to smoke or ingest modafinil to produce a strong high, so the possibility of abuse is lower. Another roadblock to wider use appeared in 2006, when the FDA rejected the drug as a treatment for ADHD in children because of reports about serious skin rashes.

Repackaging old attention-boosting drugs as cognitive enhancers for students, executives and

[A LONG HISTORY]

A WARRIOR'S LITTLE HELPER

The notion that a pill could improve mental and physical performance in healthy people gained credence during World War II. Both sides in the conflict consumed millions of amphetamines, such as these "wakey wakey" pills distributed by a British Royal Air Force medical officer to a member of a bomber flight crew.



LUCY READING-IKKANDA (*pills*); COURTESY OF COMMONWEALTH AIR TRAINING PLAN MUSEUM (*photograph*)

New enhancers may derive from the biochemical processes underlying memory formation.

software programmers may produce only marginal benefits over consuming a double espresso. The question of what exactly is an enhancer has prompted the convening of a group within the American College of Neuropsychopharmacology to discuss the standards that any drug should meet to be classified as a cognitive booster. Ultimately, enhancement drugs may come from another sphere of research. Insights into how we translate a baby's image or a friend's name into lasting memories has laid the groundwork for new drugs specifically designed to achieve better functioning in people with Alzheimer's or other dementias.

Optimism about a new generation of pharmaceuticals derives in part from advances in basic research into the biochemical processes underlying memory formation. More than 30 types of gene-altered mice have demonstrated the ability to both acquire information and store it in long-term memory better than the average mouse. "This is the first time in the history of neuroscience that we have the backbone of the molecular and cellular biology of memory," says Alcino J. Silva, a neurobiologist at the University of California, Los Angeles. "What this means for society is that for the first time we can use it to start changing how we learn and remember."

But truly effective memory drugs are probably a long way off, in part because of the scientific challenges. Most of the 200 gene mutations introduced into mice by researchers worldwide caused deficits. Silva remembers one mouse in his laboratory that illustrated the possible tradeoffs that researchers will confront during development of a cognitive enhancer. The animals learned faster than normal, unaltered mice but were unable to complete an elaborate puzzle administered by the investigators. "If you taught them something simple, they acquired it fast, but for anything more complicated, they couldn't acquire it," Silva says. He estimates that it may take decades before drugs from this research are routinely used.

The logistical challenges are daunting as well. Several of the first companies to enter the fray, including ones founded by leading academics, have faltered. In 2004 *Science* magazine cited four new firms—Sention, Cortex Pharmaceuticals, Memory Pharmaceuticals and Helicon Therapeutics—as exemplars of a trend. Sention went out of business. Cortex is ailing and desperately seeking a partner. Last year Hoffmann–La Roche purchased at a penny-stock price (less than $1) Memory, co-founded by Nobelist Kandel, after it had experienced layoffs and a number of failed clinical trials. Helicon has survived because of the largesse of billionaire Kenneth Dart, the Styrofoam cup magnate, who was enticed by the prospect of memory drugs—the company has been developing a drug that would modulate a pathway related to glutamate, a neurotransmitter that triggers an intricate cellular signaling path related to the formation of long-term memories [*see box on opposite page*].

A sister company, Dart NeuroScience, now handles development of new drug candidates, leaving the job of conducting clinical trials to Helicon. So far Helicon has received more than $100 million in funding but has yet to reach late-stage clinical trials for any of its drug candidates. "The way I like to explain this to audiences when I give talks is that when Helicon was formed I thought that I was making memory enhancers for my parents and I had no gray hair," says Tim Tully, Helicon's chief scientific officer, who co-founded the company when he was at Cold Spring Harbor Laboratory. "They're now

[IN THE PIPELINE]

PROSPECTS FOR ENHANCERS

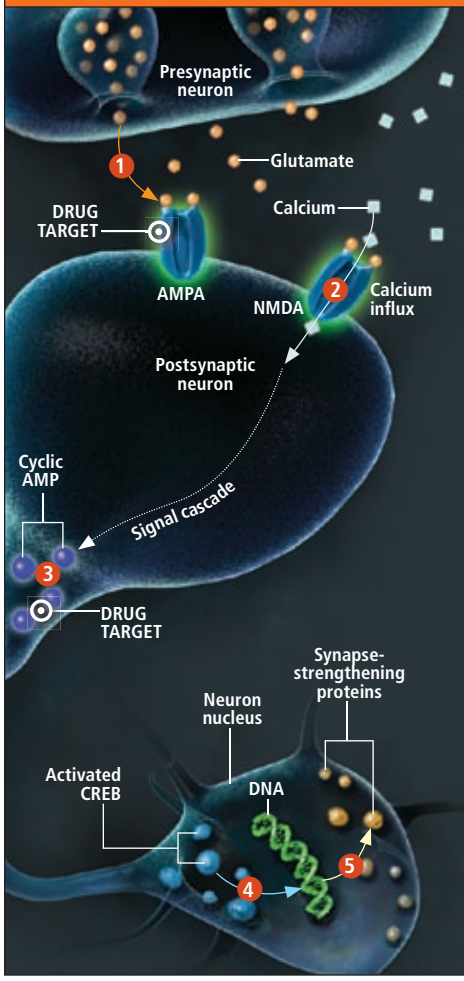
Drugmakers have plans to counter various forms of dementia, ranging from that found in Alzheimer's disease to the common memory loss that occurs with aging (age-associated memory impairment). These compounds, a selection of which are included here and many of which have yet to reach late-stage clinical trials, might eventually be used by healthy people who want to improve mental functioning, although questions remain about how safe or effective they would be for people without a cognitive deficit.

DRUG CLASS	HOW IT WORKS	DEVELOPERS
Nicotinic acetylcholine receptor activators	Either increase levels of the neurotransmitter acetylcholine in the synapse of a neuron, or the drugs themselves take the place of acetylcholine in the synapse to activate the nicotinic acetylcholine receptor, enhancing attention, memory and other facets of cognition	Abbott, CoMentis, EnVivo, Targacept/AstraZeneca and Xytis
Ampakines	Act on AMPA receptors to strengthen neuronal responses to the neurotransmitter glutamate, activity that should facilitate the laying down of long-term memories [*see box on opposite page*]	Cortex Pharmaceuticals; Eli Lilly, GlaxoSmithKline/ Neurosearch, Organon, Pfizer and Servier
Phospho-diesterase (PDE) inhibitors	One type of PDE blocker enables a signaling molecule, cyclic AMP, to remain active longer in brain neurons, thereby enhancing the activity of a protein called CREB that is important to long-term memory [*see box on opposite page*]	Helicon Therapeutics, Hoffmann–La Roche and Merck
Antihistamines	Block a histamine receptor called the H3 receptor, thereby improving wakefulness, attention and cognition. One drug that interacts with the H1 receptor, developed as a treatment for hay fever in Russia, has entered late-stage clinical trials as an enhancer	GlaxoSmithKline, Johnson & Johnson and Medivation/Pfizer

LUCY READING-IKKANDA (*pills*)

[MAKING BETTER MEMORIES]

DRUGS TO REMEMBER



Researchers have labored, in one instance for almost 20 years, on drugs that enhance cognition by acting on molecules involved in long-term memory.

Neuroscientists postulate that long-term memory involves attachment of the neurotransmitter glutamate to two types of receptors on recipient neurons. After the AMPA receptor is bound 1, it leads the other bound receptor—the NMDA type—to open a channel, allowing an influx of calcium 2. Calcium sets off a train of signaling that activates a molecule, cyclic AMP 3, which, in turn, switches on other molecules that migrate to the cell's nucleus and turn on the CREB protein 4. CREB acts on DNA in a way that triggers synthesis of proteins that then move back to the synapse and strengthen the signaling connection between the glutamate-emitting and glutamate- receiving neurons 5. Drugs that make this process more efficient—either by enhancing signaling through AMPA receptors or by keeping cyclic AMP working longer—have gone through a few clinical trials.

dead, I'm fully gray, and I'm fully cognizant of the fact that this is a race for me not them."

Tully, 55, adds that he does not foresee his creations ever becoming the next Viagra or Prozac. "What the media loves to totally ignore is the side-effect potential and jump right to the wild speculation of this as a lifestyle drug," Tully says. "And I think it's just missing the mark. The reality is that if you've got a debilitating form of memory impairment these drugs may be helpful, but they're probably going to be too dangerous for anyone else."

Despite these cautionary tales, drugmakers continue trying to develop cognitive enhancers for Alzheimer's and other dementias [*see table on opposite page*]. Among the compounds under consideration are ones that alter the effects of neurotransmitters other than glutamate—including receptors switched on by the nicotine in tobacco (though not the one linked to addiction). One of the reasons that people smoke is because nicotine helps to sharpen attention.

MORE TO EXPLORE

Memories Are Made of This: How Memory Works in Humans and Animals. Rusiko Bourtchouladze. Columbia University Press, 2002.

Towards Responsible Use of Cognitive-Enhancing Drugs by the Healthy. Henry Greely et al. in *Nature,* Vol. 456, pages 702–705; December 11, 2008.

The Molecular and Cellular Biology of Enhanced Cognition. Yong Seok Lee and Alcino J. Silva in *Nature Reviews Neuroscience,* Vol. 10, pages 126–140; February 2009.

The Future of Psychopharmacological Enhancements: Expectations and Policies. Maartje Schermer et al. in *Neuroethics,* Vol. 2, pages 75–87; July 2009.

Lessons learned from drugs developed for dementia could lead to agents that ease the milder cognitive problems associated with normal aging, assuming these compounds do not arrive burdened with intolerable side effects. If sufficiently benign, these pills could find their way into college dorms or executive suites. "Within the pharmaceutical field, people recognize that a successful cognitive enhancer could be the best-selling pharmaceutical of all time," says Peter B. Reiner, a professor of neuroethics at the University of British Columbia.

Near to Market

As scientifically satisfying as it would be for researchers to discover cognition-enhancing drugs through detailing the molecular processes that underlie cognition, the first new agents to reach the market for dementia and other cognitive disorders may not spring from deep insight into neural functioning. They may come from the serendipitous discovery that some compound approved for another purpose has effects on cognition. For instance, one drug candidate that recently entered late-stage trials for the cognitive dysfunctions of Alzheimer's was developed in Russia as an antihistamine for hay fever and was later found to have antidementia properties. The potentially huge market has led some companies to take unorthodox routes to market, revisiting a failed drug or one that did not complete clinical trials and selling it as a dietary supplement or as a less stringently regulated "medical food."

Similarly, new medicines may arrive because regulatory agencies approve a broadening of allowed uses for a drug already known to influence cognition. Cephalon, maker of modafinil, took this route, obtaining FDA permission to market the substance for shift workers, who compose a much larger group than the narcoleptics (who suffer from uncontrolled sleep episodes) for whom it was originally approved. (Cephalon also paid nearly $444 million to two states and the federal government for promoting three drugs, including modafinil, for unapproved uses.) The impulse to improve cognition—whether to intensify mental focus or to help recall a friend's phone number—may prove so compelling to both drugmakers and consumers that it may overshadow the inevitable risks of toying with the neural circuitry that imbues us with our basic sense of self. ■

Gary Stix is a writer at Scientific American.

ANDREW SWIFT

SQUEEZING MORE OIL FROM THE GROUND

Amid warnings of a possible "peak oil," advanced technologies offer ways to extract every last possible drop

BY LEONARDO MAUGERI

LANCE IVERSEN *Corbis*

KEY CONCEPTS

- Forecasts that global oil production will soon start to decline and that most oil will be gone within a few decades may be overly pessimistic.
- The author predicts that by 2030, thanks to advanced technologies, wells will be able to extract half of the oil known to be underground, up from the current average of 35 percent.
- Together with new discoveries, the increased productivity could make oil last at least another century.

—The Editors

On fourteen dry, flat square miles of California's Central Valley, more than 8,000 horsehead pumps—as old-fashioned oilmen call them—slowly rise and fall as they suck oil from underground. Glittering pipelines crossing the whole area suggest that the place is not merely a relic of the past. But even to an expert's eyes, Kern River Oil Field betrays no hint of the technological miracles that have enabled it to survive decades of dire predictions.

When Kern River Oil Field was discovered in 1899, analysts thought that only 10 percent of its unusually viscous crude could be recovered. In 1942, after more than four decades of modest production, the field was estimated to still hold 54 million barrels of recoverable oil, a fraction of the 278 million barrels already recovered. "In the next 44 years, it produced not 54 [million barrels] but 736 million barrels, and it had another 970 million barrels remaining," energy guru Morris Adelman noted in 1995. But even this estimate proved wrong. In November 2007 U.S. oil giant Chevron, by then the field's

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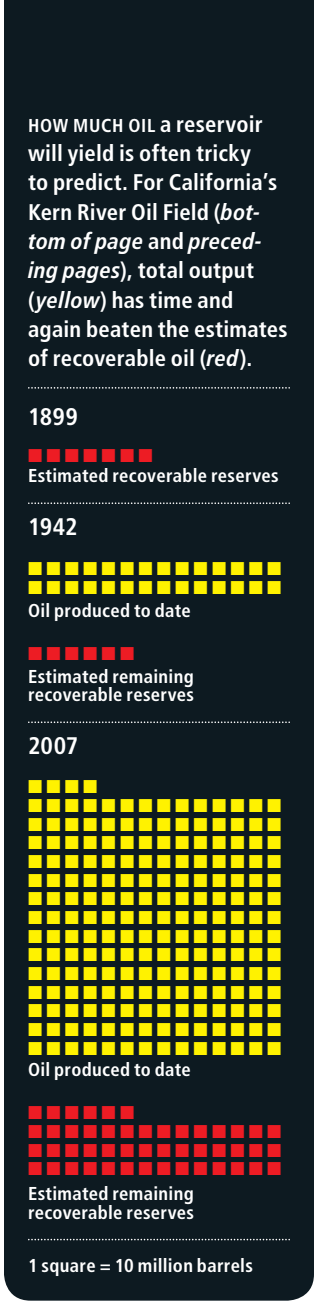


operator, announced that cumulative production had reached two billion barrels. Today Kern River still puts out nearly 80,000 barrels per day, and the state of California estimates its remaining reserves to be about 627 million barrels.

Chevron began to markedly increase production in the 1960s by injecting steam into the ground, a novel technology at the time. Later, a new breed of exploration and drilling tools—along with steady steam injection—turned the field into a kind of oil cornucopia.

Kern River is not an isolated case. According to common wisdom, a field's production should follow a bell-shaped trajectory known as the Hubbert curve (after the late Shell Oil geologist M. King Hubbert) and peak when half of the known oil has been extracted. Instead most of the world's oil fields have revived over time. In a way, technology is the real cornucopia.

Many analysts now prophesy that global oil production will peak in the next few years and then decline, following the Hubbert curve. But I believe that those projections will prove wrong, just as similar "peak oil" predictions [see "The End of Cheap Oil," by Colin J. Campbell and Jean H. Laherrère; Scientific American, March 1998] have been mistaken in the past. New exploration methods have revealed more of the earth's secrets. And leaps in extraction technology have led to tapping oil in once inaccessible areas and in places where drilling used to be uneconomic. Advanced exploration and extraction methods can keep oil production growing for decades to come and could allow oil supplies to last at least another century.

Although oil and other fossil fuels pose risks for the climate and the environment, for now alternative energy sources cannot compete with their versatility, cost, and ease of transport and storage. As research into alternatives goes on, we will need to be sure that we use the oil we have responsibly.

All That You Can't Leave Behind

At a time when the world increasingly fears an approaching peak and subsequent decline in oil production, it may be surprising to learn that most of the planet's known resources are left unexploited in the ground and that even more still wait to be discovered.

On the face of it, oil should last only a few more decades. In 2008, just before the economic meltdown slashed consumption, the world burned about 30 billion barrels of oil a year. Assuming that in the near future consumption resumed at 2008 levels and then stayed constant, our planet's proven reserves of oil—currently estimated at between 1.1 trillion and 1.3 trillion barrels—would have about 40 years to go.

But proven reserves are only estimates and not fixed numbers. They are defined as the amount of known oil that can be recovered economically with current technology, so the definition changes as technology develops and as the price of crude varies. In particular, if supply tightens or demand increases, resale prices go up, and oil that was once too expensive to extract becomes part of the proven reserves. That is why most oil fields have produced much more than the initial estimates of their reserves assumed and even more than the initial estimates of their total content. Today only 35 percent of the oil in the average oil field is recovered, meaning that about two thirds of the oil in known fields remains underground. That resource is rarely mentioned in the debate on the future of oil.

Even a mature oil country such as the U.S.,

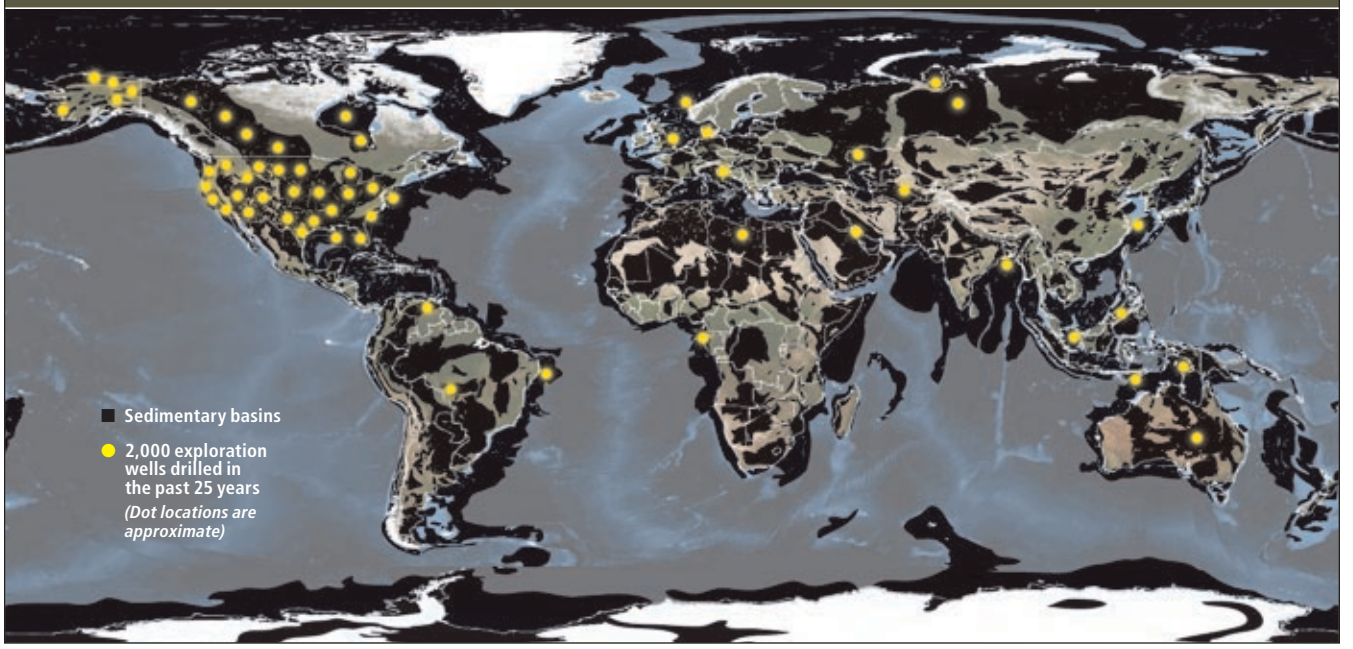
SCIENTIFIC AMERICAN; SOURCE: LEONARDO MAUGERI (*chart*); DAVID McNEW *Getty Images* (*photograph*)

Kern River Oil Field

[EXPLORATION PROSPECTS]

UNCHARTED LANDS (AND SEAS)

Oil is found in sedimentary rock on continents and continental shelves. Much of the surface of the earth's continental plates is known to contain sedimentary basins (*black*). Only one third of this surface, however, has been searched for oil with modern techniques, which, for instance, can locate reservoirs that lie under salt deposits thousands of meters thick. Far more exploration wells (*each yellow dot represents 2,000*) have been drilled in the U.S. than in any other country.



whose oil production has been declining since the 1970s (if not as fast as the Hubbert curve predicted), still holds huge volumes of unexploited oil under its surface. Although the country's proven oil reserves are now only 29 billion barrels, the National Petroleum Council (NPC) estimates that 1,124 billion barrels are still left underground, of which 374 billion barrels would be recoverable with current technology.

On a global scale, the U.S. Geological Survey estimates the earth's remaining conventional oil (petroleum) deposits to be around seven trillion to eight trillion barrels. But with today's technology, know-how and prices, only part of that oil can be recovered economically and is thus classified as a proven reserve.

And there is more.

Only one third of the sedimentary basins of our planet—the geologic formations that may contain oil—has been thoroughly explored with modern technologies [*see map above*]. Moreover, the USGS data do not include unconventional oils, such as ultraheavy oils, tar sands, oil shales and bituminous schist, which together are at least as abundant as conventional oil.

Thus, a country or a company may increase its reserves of black gold even without tapping new areas and frontiers, if it is capable of recovering more oil from known fields. Still, doing so is not always easy.

A Rocky Start

Contrary to common belief, oil is not held in great underground lakes or caves. If you could "see" an oil reservoir, you would notice only a rocky structure seeming to have no room for oil. But beyond the reach of the human eye, a world of often invisible pores and microfractures entraps minuscule droplets of oil, together with water and natural gas.

Nature created these formations over millions of years. It started when huge deposits of vegetation and dead microorganisms piled up at the bottom of ancient seas, decomposed and became buried under successive layers of rock. High temperatures and pressures then slowly transformed the organic sediments into today's oil and gas. These fossil fuels soak the porous underground rock almost like water soaks pumice.

When such a reservoir is drilled, it behaves a bit like an uncorked bottle of champagne. The oil is freed from its ancient rocky prison, and the reservoir's internal pressure pushes it to the surface (along with stones, mud and other debris). The process goes on until the pressure peters out, usually after several years. This initial, or

Most of the planet's known resources are left unexploited in the ground, and more still wait to be discovered.

JEN CHRISTIANSEN; SOURCES: IHS PEPS/E&P STATISTICS; IHS EDIN-GIS DATABASE (WWW.IHS.COM/ENERGY)

primary, stage of recovery can usually yield between 10 and 15 percent of the oil in place. From then on, recovery must be assisted.

About one third of the oil left in a reservoir after the initial "champagne" release is called immobile oil—drops trapped by strong capillary forces within isolated pores in the rock. No technique exists yet to extract this part of the oil. The remaining two thirds, though mobile, will not necessarily flow into the wells on its own. In fact, usually about half of the mobile oil stays stuck inside the reservoir because of geologic barriers or low permeability, which happens when the pores are too narrow. The situation is even worse when the oil is not a light liquid but a heavy, viscous, molasseslike substance.

To help some of the remaining oil seep through the pores in the rock and come out of the wells, operators usually inject natural gas and water into the reservoir, in what is called secondary recovery. Injecting gas restores the lost pressure and forces oil that is sufficiently fluid to seep through the rock's pores. Meanwhile, because oil is lighter than water, injection of water raises the oil toward the well, just like pouring water in a glass filled with olive oil would send the oil upward.

In the past decade or so, the distinction between primary and secondary recovery has blurred as companies have begun to apply advanced technology from the outset. One of the most important developments so far has been the horizontal well, an L-shaped structure able to deliver dramatically more oil than the traditional vertical drilling that has been used since the inception of the oil industry. The L shape enables horizontal wells to change direction and penetrate sections of a reservoir that would otherwise be unreachable. The method, first adopted commercially in the 1980s, is particularly suitable in reservoirs where oil and natural gas occupy thin, horizontal layers.

Exploration tools have also improved over the years. Advanced 3-D imaging of the underground, for instance, which is based on how seismic waves bounce off the boundaries between

[THE AUTHOR]

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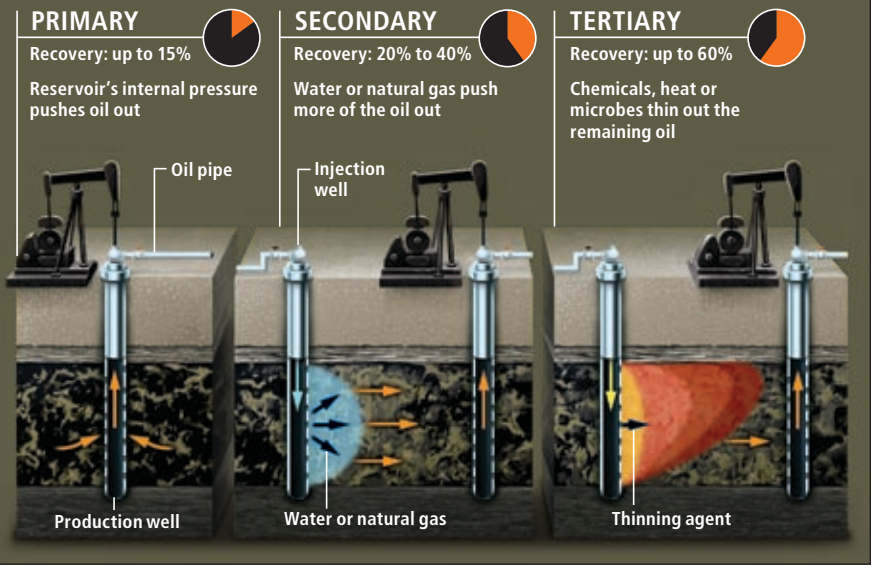
▲ Oil reservoirs are not underground lakes, but layers of oil-soaked porous rock. This five-centimeter-tall core comes from offshore fields near Sicily that are too expensive to develop with current technology. Its thick veins of oil feel solid to the touch, as if the white, carbonate rock were simply stained.

[THE BASICS]

THREE STAGES OF RECOVERY

Only 10 to 15 percent of the oil in a reservoir gushes out spontaneously after drilling (*primary recovery, below left*). Once the internal pressure peters out, pumping water or natural gas into the ground forces more oil out (*secondary recovery, center*), so that 20 to 40 percent of the original oil can be extracted. The remaining oil is either trapped in small, isolated pockets—and thus unrecoverable—or too viscous to flow toward the wells. But more advanced technologies [*see box on opposite page*] can thin out the viscous oil and bring total yield to as much as 60 percent or more (*tertiary recovery, right*).



COURTESY OF LEONARDO MAUGERI (*author*); COURTESY OF DARIO SPERANZA (*rock sample*); JEN CHRISTIANSEN (*illustration*)

layers of different rock composition, now offers more detailed understanding of the structure of existing fields, which helps in choosing where to drill to optimize recovery.

Imaging technologies now enable geologists to "see" what lies underneath layers of salt that sit unevenly distributed below the seabed and are sometimes thicker than 5,000 meters. Similar to frozen waters, salt formations used to represent a formidable obstacle because they blurred the seismic waves used to reconstruct an accurate image of the underground.

Such imaging breakthroughs, combined with more advanced offshore technologies, have made new parts of the oceans accessible to oil developers. At the time when the North Sea oil fields were developed in the 1970s, it seemed as if offshore technology had reached its most daunting milestone, tapping fields that lay below 100 to 200 meters of water and 1,000 meters under the seabed. But in the past few years the industry has succeeded in striking oil at depths below 3,000 meters of water and 6,000 meters of rock and salt. There have been at least three major ultradeep offshore discoveries: Thunder Horse and Jack in the Gulf of Mexico and Tupi off the coast of Brazil.

[TERTIARY RECOVERY TECHNIQUES]

UNCONVENTIONAL WEAPONS

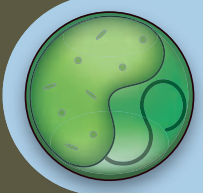
After primary and secondary recovery have run their course, more aggressive methods, some of them still experimental, can soften the remaining oil so it can flow toward the wells. Because these advanced methods are expensive, the battle to get more out only gets this fierce when resale prices are sufficiently high.

INCENDIARY

Burning part of a reservoir (which requires injecting air underground) enhances the recovery rate in three ways. First, heat from the fire makes oil less viscous. Second, the combustion produces carbon dioxide, which pushes oil out. Third, the fire breaks the larger and heavier molecules of oil, making it more mobile.

CHEMICAL

Substances called surfactants, injected into a reservoir, help oil detach from the rock and flow better. Layers of surfactant engulf oil into droplets, similar to the way ordinary soap washes oily materials off a surface. A variation consists of injecting chemicals that generate the soaplike materials from components present within the oil itself.



BIOLOGICAL

Experiments are testing the injection of bacteria (together with nutrients and, in some cases, oxygen) that grow in the interface between the oil and the rock, helping to release the oil. The bacteria are allowed to grow for several days before recovery resumes. In the future, genetically engineered microorganisms could partially digest the most viscous oil and thin it out.

Scraping the Barrel

As wells have gone farther and deeper than ever before, technologies have also evolved to get more oil out of the rock after the first lines of recovery have run their course. Primary and secondary recovery stages together can bring the recovery rate to between 20 and 40 percent. To go beyond that, in what experts call tertiary recovery, it is usually necessary to make the remaining oil less viscous, which can be accomplished using heat, gases, chemicals and even microbes. Steam injection, among the oldest heat-based methods, was decisive in the revival of the Kern River Oil Field back in the early 1960s. The injected steam heats the overlying formation and enables oil to move. To this day, Kern River's steam-injection project is among the largest of its kind in the world. A variant of steam-assisted recovery has been applied to tar sand deposits in Alberta that are too deep to be surface-mined.

Another heat-based process that has been tested in the field is burning a part of the reservoir's hydrocarbons by igniting it with a heater while pumping air into a well to feed the combustion. The fire generates heat and carbon dioxide (CO_2), both of which make oil less viscous; much of the CO_2 also remains underground and helps to push the oil out. At the same time, the fire itself breaks the larger and heavier molecules of oil, once again making it mobile. The airflow can be controlled to limit oil that gets burned and to prevent the release of pollution into the surrounding environment.

Advanced exploration and extraction methods can keep oil production growing for decades to come.

A more common method is the high-pressure injection of gases such as CO_2 or nitrogen into the reservoir. These gases can restore or maintain a reservoir's pressure and can also mix with oil, reducing both its viscosity and the forces that can keep the oil trapped. In the U.S., CO_2 extracted from volcanoes or from waste gases from power stations has been applied to oil recovery since the 1970s. The process is in use in about 100 ongoing projects, with dedicated pipeline networks totaling more than 2,500 kilometers.

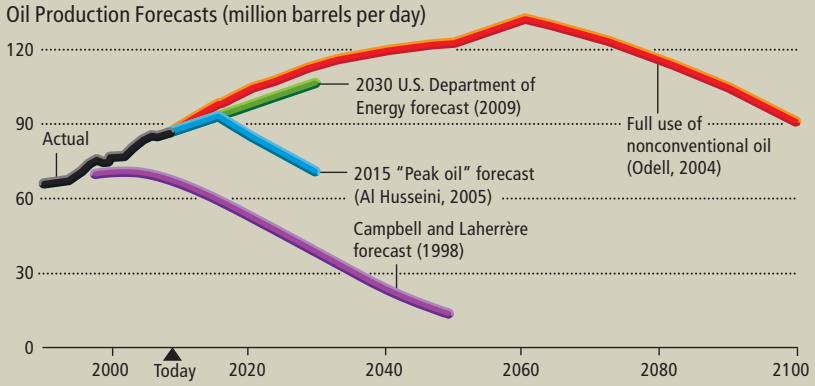
The know-how accumulated in CO_2 injection has opened the way for the capture and storage of CO_2 from power plants—procedures that could help slash emissions of this greenhouse gas into the atmosphere and instead keep it underground for hundreds of years. The first commercial carbon capture and storage project has been active at the Sleipner field, off the coast of Norway, since 1996, and is storing one million met-

JEN CHRISTIANSEN

PREDICTIONS VARY WIDELY for the world's future production of oil. Some analysts have used a model originally proposed by geologist M. King Hubbert to predict a bell-shaped curve peaking around the year 2002 (*purple*), or, more recently, 2015 (*blue*), and then declining inexorably. Other, more optimistic forecasts, such as one by the U.S. government (*green*), take into account expectations for the discovery of new oil fields and technology's push to get more oil out of old fields. Full development of nonconventional sources such as tar sands and oil shales might keep the curve rising for another five decades (*red*).

HOW MUCH OIL IS LEFT?

Oil Production Forecasts (million barrels per day)



TAR SANDS are among the most abundant potential sources of nonconventional oil. Exploiting them, however, is energy-intensive and and may have serious environmental side effects, including the production of large amounts of wastewater.

ric tons of CO_2 a year. This amount is small, considering that human activity alone is estimated to eject into the atmosphere greenhouse gases equivalent to around 50 billion metric tons of carbon dioxide every year. But the plant's success serves as a proof of concept.

Ironically, however, one of the main problems with using CO_2 for oil recovery is its scarcity. Capturing the gas from power station smokestacks or volcanoes is not cheap, and the cost of capturing it from smaller sources, such as cars or even most industrial plants, is prohibitive. Another hurdle is transportation, which can be too costly if the oil fields are in remote regions.

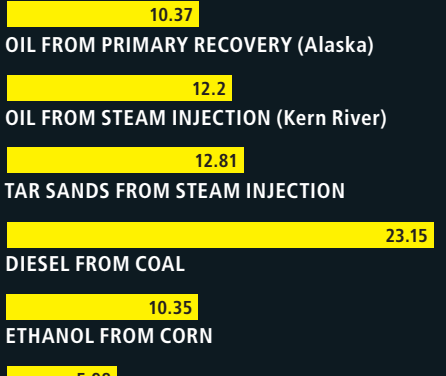
Chemistry-based recovery is a more recent strategy. Certain chemicals can mix with trapped oil and make it less viscous, so that it can flow toward the well. These substances all work on the same principle, which is similar to how layers of soap molecules engulf fatty substances and work to remove grease from your hands. The most successful chemical process also increases the viscosity of the underground water, which helps the water push the oil toward the wells without reaching the wells first. At China's Daqing oil field, this process is credited for getting out an extra 10 percent of the reservoir's oil since the mid-1990s. And in one version of the process, a caustic solution generates the soaplike materials from components present within the oil itself, limiting the overall cost.

Microbial enhanced oil recovery is still in its infancy, with experiments under way in the U.S., China and other countries . Engineers pump vast amounts of specialized microbes into the reservoir, together with nutrients and, in some cases, oxygen. The microbes grow in the interface between the oil and the rock, helping to release the oil. Genetic engineering opens up the possibility of modifying bacteria and other microorganisms to make them more efficient at aiding oil recovery.

None of these advanced recovery techniques is particularly cheap. But some (notably CO_2-assisted recovery, if a source of the gas is easily accessible nearby) are already economical as long as the price of crude stays above $30 per barrel,

CARBON FOOTPRINT of burning a gallon of fuel depends on myriad factors, including how the raw material is extracted and processed. Recovering viscous oil by injecting steam into the ground requires additional energy as compared with pumping out "easy oil" and results in more CO_2 (carbon dioxide) emissions. So does extracting oil from tar sands. But converting coal into diesel fuel has by far the heaviest associated emissions.

CO_2 EMISSIONS (kilograms of CO_2 per gallon of gasoline or per equivalent amount of other fuel)



JEN CHRISTIANSEN; SOURCES FOR TOP GRAPH: "WHY CARBON FUELS WILL DOMINATE THE 21ST CENTURY'S GLOBAL ENERGY ECONOMY," BY PETER R. ODELL, MULTI-SCIENCE PUBLISHING, 2004 (*red curve*); U.S. DEPARTMENT OF ENERGY, REPORT #DOE/EIA-0484, 2009 (*green curve*); AL HUSSEINI, BASED ON 2005 INTERVIEW WITH ASPO-USA (*2015 peak forecast, blue curve*); ASSOCIATION FOR THE STUDY OF PEAK OIL AND GAS (ASPO) NEWSLETTER, COMPILED BY C. J. CAMPBELL, NO. 90; JUNE 2008 (*2010 peak, purple curve*); SOURCES FOR BOTTOM CHART: "TRANSPORTATION IN A CLIMATE-CONSTRAINED WORLD," BY ANDREAS SCHÄFER ET AL., MIT PRESS, 2009; "COMPARISON OF NORTH AMERICAN AND IMPORTED CRUDE OIL LIFECYCLE GHG EMISSIONS," BY JEFF ROSENFELD, JENNIFER PONT AND KAREN LAW, IN *TIAX LLC REPORT*, JULY 6, 2009; "ENVIRONMENTAL, ECONOMIC, AND ENERGETIC COSTS AND BENEFITS OF BIODIESEL AND ETHANOL BIOFUELS," BY JASON HILL, ERIK NELSON, DAVID TILMAN, STEPHEN POLASKY AND DOUGLAS TIFFANY, IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 103, NO. 30; JULY 25, 2006; LARA SOLT *Corbis (hands holding tar sands)*

Peak or No Peak?

Many observers fret about the future availability of oil and whether the relentless growth in global oil production is reaching its end. The author is a professed skeptic; we asked him to elaborate.

***SCIENTIFIC AMERICAN*: You have often said publicly that cries about the impending "peak oil" are excessively alarmist. But isn't it better to be safe than sorry?**

LEONARDO MAUGERI: It is absurd to predict a peak of world production because it presupposes that one knows how much oil is in the ground. But no one actually knows what the total amount is—not even its order of magnitude. Meanwhile the worst effect of this recurring oil panic is that it drives Western political circles toward attempts to assert control over oil-producing regions.

SA: But peak oilers point to the recent instability of the price of crude (it went from a peak of $147 per barrel in July 2008 to around $32 in December and then back to $70 in August 2009) as a sign that we are nearing the peak.

LM: If everyone thought that oil was running out, the price would go up relentlessly, instead of fluctuating. And because the price of oil sets the prices of all sources of energy, the uncertainty hurts everyone—look at what has happened to the investment in renewable energy since the end of 2008!

SA: Indeed, major projects, such as oil tycoon T. Boone Pickens's plan for a wind farm in Texas, have been put on hold. So why the price swings?

LM: My theory is that the expected spare production capacity—or lack thereof—is what drives the cycles in oil prices. The problem is that you cannot change the size of spare capacity overnight.

SA: What can be done to stabilize prices?

LM: At the meeting of the energy ministers of the G8 this past May, Eni, my company, proposed the establishment of a Global Energy Agency with a mandate to reduce oil price volatility. Its main task would be to supply comprehensive and transparent data about the oil market and to run both a global stabilization fund to prevent oil prices from crashing and a market of spare capacity to prevent them from skyrocketing.

SA: From the environmental point of view, are high oil prices good or bad?

LM: The world needs an oil price that is neither too high nor too low. In today's conditions, the ideal price would be between $60 and $70. At prices above $70, inefficient methods of producing biofuel become profitable, for example, turning corn into ethanol. Biofuel production then tends to displace global agriculture, with devastating effects on the world's poorest people. Below $50 or $60, conservation is left aside, and renewable source projects vanish.

and most, including chemistry-based recovery, become economical at around $50 per barrel.

Future Eurekas

"Easy oil" is running out, probably because it was the first to be discovered and burned. Many of the largest and most productive oil basins in the world are approaching what I call technological maturity, which is when traditional technologies stop being effective. These basins include reservoirs in Persian Gulf countries, Mexico, Venezuela and Russia that started yielding oil in the 1930s, 1940s and 1950s. For these fields to keep producing in the future, new technologies will be required.

But "easy oil" wasn't so "easy" when it was discovered. By the same token, the difficult oil of today will be tomorrow's easy oil, thanks to the learning curve of technology expertise. Technological breakthroughs in the oil industry have always been the result of long, drawn-out processes. Horizontal drilling was first tested in the 1930s, and some of the more advanced recovery methods have existed at least since the 1950s. For most of the industry's history, however, oil has been overabundant, so its price has been too low to justify significant and costly innovations. But a new era is coming in which new technologies will be adopted at a faster pace.

The move toward increased recovery rates may be slowed down by the current wave of resource nationalism. Whereas in the early 1970s the major oil companies controlled around 80 percent of global oil reserves, today more than 90 percent of the world's conventional oil is under the direct control of producing countries, through their national oil companies. But the uncertain future of the demand for oil makes some of these countries reluctant to invest in modern technology and in exploration, especially because making significant investments means taking resources away from social and economic development programs.

Still, I dare to make a prediction. By 2030 more than 50 percent of the oil known at the time will be recoverable. Also, by that time the amount of known oil will have grown significantly, and a larger portion of unconventional oils such as oil shales will be commonly produced, bringing the total amount of recoverable reserves to something between 4,500 billion to 5,000 billion barrels of oil. A significant part of the "new reserves" will not come from new discoveries but from a new ability to better exploit what we already have.

To be sure, by 2030 we will have consumed another 650 billion to 700 billion barrels of our reserves, for a total of around 1,600 billion barrels used up from the 4,500-billion to 5,000-billion figure. Yet if my estimates are correct, we will have oil for the rest of the 21st century. The real problem will be how to use the remaining oil without wasting it through unacceptable consumption habits and—above all—without endangering the environment and climate of our planet. ■

MORE TO EXPLORE

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Lost Cities of the Amazon

The Amazon tropical forest is not as wild as it looks

By Michael J. Heckenberger

LUIGI MARINI

KEY CONCEPTS

- To most people, the Amazon forest is the quintessential case of pure nature slowly being destroyed as humans intrude.
- In fact, what seems pristine has itself been shaped by humans. In some areas the forest is secondary growth that took hold when native peoples were wiped out by their encounters with Europeans. The author and his colleagues have found extensive pre-Columbian ruins. Communities had a self-similar or fractal structure in which houses, settlements and clusters of settlements were organized in similar ways.
- Thus, the history of the Amazon is rather more interesting than usually thought. The environmental challenge is not only to preserve unspoiled wilderness but also to recover the techniques of sustainable farming and forestry that the ancestors of the region's present inhabitants developed.

—The Editors

When Brazil established the Xingu Indigenous Park in 1961, the reserve was far from modern civilization, nestled deep in the southern reaches of the vast Amazon forest. When I first went to live with the Kuikuro, one of the reserve's principal indigenous groups, in 1992, the park's boundaries were still largely hidden in thick forest, little more than lines on a map. Today the park is surrounded by a patchwork of farmland, its borders often marked by a wall of trees. For many outsiders, this towering green threshold is a portal, like the massive gates of Jurassic Park, between the present—the dynamic modern world of soy fields, irrigation systems and 18-wheelers—and the past, a timeless world of primordial nature and society.

Long before taking center stage in the world's environmental crisis as the giant green jewel of global ecology, the Amazon held a special place in the Western imagination. Mere mention of its name conjures images of dripping, vegetation-choked jungles; cryptic, colorful and often dangerous wildlife; endlessly convoluted river networks; and Stone Age tribes. To Westerners, Amazonian peoples are quintessential simple societies, small groups that merely make do with what nature provides. They have complex knowledge about the natural world but lack the hallmarks of civilization: centralized government, urban settlements and economic production beyond subsistence. In 1690 John Locke famously proclaimed, "In the beginning all the World was America." More than three centuries later the Amazon still grips the popular imagination as nature at its purest, home to native peoples who, in the words of *Rolling Stone* editor Sean Woods in October 2007, preserve "a way of life unchanged since the dawn of time."

Looks can be deceiving. Hidden under the forest canopy are the remnants of a complex pre-Columbian society. Working with the Kuikuro,

I have excavated a network of ancestral towns, villages and roads that once supported a population perhaps 20 times its present size. Huge swaths of forest have grown over the ancient settlements, gardens, fields and orchards, which fell into disuse when epidemics brought by European explorers and colonists decimated the native peoples. The region's rich biodiversity reflects past human intervention. By developing a mix of land uses, soil-enrichment techniques and long crop rotation cycles, the ancestors of the Kuikuro thrived in the Amazon despite its infertile natural soils. Their accomplishments could inform efforts to reconcile the environmental and development goals of this region and other parts of the Amazon.

KUHIKUGU, known to archaeologists as site X11, is the largest pre-Columbian town yet discovered in the Xingu region of the Amazon. It housed 1,000 or more people and served as the hub of a network of smaller towns. For a key to this artist's conception, see page 68.

"Nature Folk"

The most famous person to go looking for lost civilizations in the southern Amazon was Percy Harrison Fawcett. The British adventurer scoured what he called the "uncharted jungles" for an ancient city, Atlantis in the Amazon, replete with stone pyramids, cobbled streets and alphabetic writing. His tales inspired Conan Doyle's *The Lost World* and perhaps the Indiana Jones movies. David Grann's gripping recent book, *The Lost City of Z,* retraced Fawcett's path before his disappearance in the Xingu in 1925.

Actually, five German expeditions had already visited the Xinguano people and lands. In 1894 Karl von den Steinen's book *Unter den Naturvölkern Zentral Brasiliens,* which described the earliest expeditions, became an instant classic in the fledgling discipline of anthropology. The book set the tone for 20th-century studies of Amazonian peoples as small, isolated groups living in a delicate balance with the tropical forest: "nature folk." Later anthropologists often viewed the forest environment as uniformly inimical to agriculture; the soil's poor fertility seemed to preclude large settlements or dense regional populations. By this reasoning, the Amazon of the past must have looked much like the Amazon in recent times.

But this view began to erode in the 1970s as scholars revisited early European accounts of the region, which talked not of small tribes but of dense populations. As Charles Mann's best-sell-

GEORGE RETSECK

[THE REGION]

Land of Legend

Archaeological surveys and excavations have revealed that parts of the Amazon were densely populated on the eve of European exploration and colonization. The author's team focuses on the area inhabited by the Kuikuro people, located in the headwaters of the Xingu River in the Brazilian state of Mato Grosso. It was here that the famous British explorer Percy Harrison Fawcett disappeared more than eight decades ago when looking for lost cities.

[WHAT THE REGION IS LIKE TODAY]

The Kuikuro

The Kuikuro people were active participants in the author's fieldwork and co-authors on the resulting journal articles. Theirs is one of the few Amazonian societies to maintain the full breadth of its culture—language, rituals, art—despite centuries of depopulation, and they continue to practice intensive agriculture (mostly of manioc), fish farming, orchard production and forest management.

◀A Kuikuro woman fishes with a basket in a pond adjacent to the archaeological site X13 (Heulugihïtï).

▼Flutists and dancers commemorate the late Brazilian anthropologist Apoena Meirelles during the Kuarup funerary festival in August 2005.

▲The Kuikuro preserve a way of life that predates 1492. The archaeological record shows that they organize their economy and settlements as their ancestors did.

▲A Xinguano village, with a population of a couple of hundred people, consists of large thatch houses around a central plaza.

ing book *1491* has eloquently described, the Americas were heavily populated on the eve of the European landings, and the Amazon was no exception. Gaspar de Carvajal, the missionary who chronicled the first Spanish expedition down the river, noted fortified towns, broad, well-kept roads and large numbers of people. Carvajal wrote on June 25, 1542:

> We went among some islands which we thought uninhabited, but after we got to be in among them, so numerous were the settlements which came into sight … that we grieved … and, when they saw us, there came out to meet us on the river over two hundred pirogues [canoes], that each one carries twenty or thirty Indians and some forty … they were colorfully decorated with various emblems, and they had with them many trumpets and drums … and on land a marvelous thing to see were the squadron formations that were in the villages, all playing instruments and dancing about, manifesting great joy upon seeing that we were passing beyond their villages.

Archaeological research in several areas along the Amazon River, such as Marajó Island at the mouth of the river and sites near the modern cities of Santarém and Manaus, has confirmed these accounts. These societies interacted in far-flung systems of trade. Less is known about the southern peripheries of the Amazon, but recent work in Llanos de Mojos in lowland Bolivia and in the Brazilian state of Acre suggests that they, too, supported complex societies. In 1720 Brazilian frontiersman António Pires de Campos described a densely settled landscape in the headwaters of the Tapajós River, just west of the Xingu:

> These people exist in such vast quantity, that it is not possible to count their settlements or villages, [and] many times in one day's march one passes ten or twelve villages, and in each one of them there are ten to thirty houses, and in these houses there are some that are thirty to forty paces across … even their roads they make very straight and wide, and they keep them so clean that one finds not even a fallen leaf….

[THE AUTHOR]

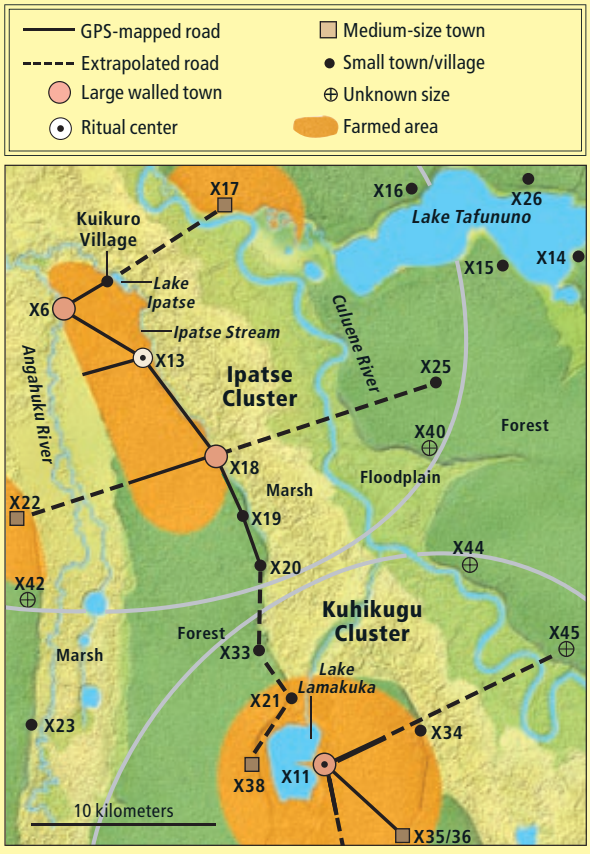
Michael J. Heckenberger has done archaeology in the Xingu region and elsewhere in the Brazilian Amazon since 1992, most recently as a professor at the University of Florida. His work focuses on the social and political organization and historical ecology of late prehistoric complex societies in the region, as well as changes in indigenous societies following European colonization not just in Brazil but also in northeastern South America, the Caribbean and northeastern North America. At home, he relaxes by cultivating bonsai.

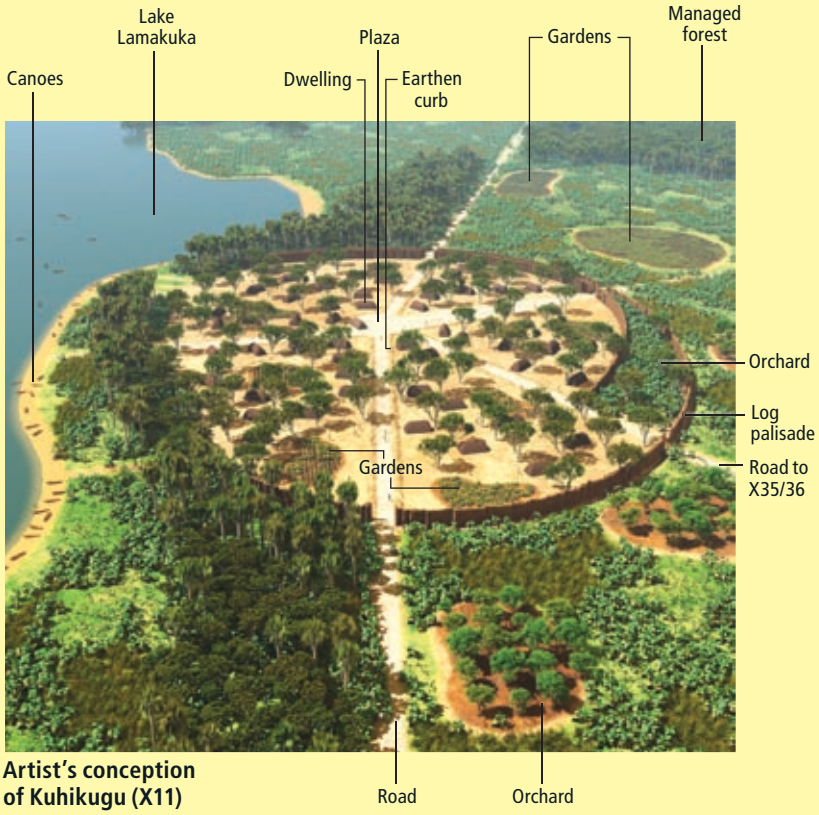
COURTESY OF MICHAEL J. HECKENBERGER (*woman fishing* and *author*); ERALDO PERES *AP Photo* (*dancing*); GREGG NEWTON *Corbis* (*child*); RICKEY ROGERS *Reuters/Corbis* (*aerial view*)

[GEOGRAPHY]

Pre-Columbian Towns

Surveys show that the Kuikuro's ancestors reworked hundreds of square kilometers of forest into productive agricultural land. Although individual settlements were small by modern standards, they were packed close together in clusters, each of which functioned as a political unit. The settlements had a fractal organization; for example, clusters, towns and houses were all organized along the same roughly east-west axis.





Artist's conception of Kuhikugu (X11)

An Ancient Walled Town

When I ventured to Brazil in the early 1990s to study the deep history of the Xingu, lost cities were the furthest things from my mind. I had read Steinen but had barely heard of Fawcett. Although much of the vast Amazon basin was archaeological terra incognito, it was unlikely that ethnographers, much less local Xinguanos, had missed a large monolithic center towering over the tropical forests.

Nevertheless, signs of something more elaborate than present-day settlements were all around. Robert Carneiro of the American Museum of Natural History in New York City, who lived with the Kuikuro in the 1950s, had suggested that their settled way of life and productive agricultural and fishing economy could support communities 1,000 to 2,000 strong—several times the contemporary population of a few hundred. He also cited evidence that indeed it once had: a prehistoric site (designated "X11" in our archaeological survey) that was surrounded by extensive ditches. The Villas Boas brothers—Brazilian *indigenistas* who were nominated for a Nobel Peace Prize for their part in creating the Xingu park—had reported such earthworks near many villages.

In January 1993, soon after I arrived in the Kuikuro village, the principal hereditary chief, Afukaka, took me to one of the ditches at a site (X6) they call Nokugu, named for the jaguar spirit being thought to live there. We passed local men who were raising a huge fish weir across the Angahuku River, which was already swelling from the seasonal rains. The ditch, which runs over two kilometers, was two to three meters deep and more than 10 meters wide. Even though I had expected to find an archaeological landscape different from today's, the scale of these ancient communities and their constructions surprised me. Kuikuro research assistants and I spent the following months mapping it and other earthworks at the 45-hectare site.

Since that time, our team has studied numer-

GEORGE RETSECK (*map*); LUIGI MARINI (*aerial view*)

ous other sites in the area, hacking more than 30 kilometers of line-of-sight transects through the forest to map, examine and excavate the sites. Many Kuikuro helped in one way or another, and some became well versed in archaeology.

At the end of 1993, Afukaka and I went back to Nokugu so I could tell him what I had learned. We followed the contour of the site's outer ditch and stopped at an earthen bridge, where a major road we had uncovered passed over it. I pointed down the arrow-straight ancient dirt road, which was 10 to 20 meters wide and led to another ancient site, Heulugihïtï (X13), about five kilometers away. We crossed the bridge and entered Nokugu.

The road, defined by low earthen curbs, widened to 40 meters—the size of a modern four-lane highway. After a couple of hundred meters, we passed over the inner ditch and stopped to look at our recently finished excavation trench, where we had found a funnel-shaped footing for a tree-trunk palisade. Afukaka told me a story of palisaded villages and raids in his people's distant past.

As we moved farther into the ancient town, we passed through patches of forest, scrub and open areas that now cover the site—the footprints of diverse past activities. We emerged into a grassy glade of towering palms marking the former plaza. I slowly spun and pointed along the perfectly circular edge of the plaza, marked by a meter-high mound. The tall palms, I told him, had colonized the plaza centuries ago from compost gardens in domestic areas.

Leaving the plaza to explore the surrounding neighborhoods, we came across large refuse middens that closely resembled the one behind Afukaka's own house. They were filled with broken pots that he noted were exactly like those his wives used to process and cook manioc, down to minute details. On a later visit, when we were excavating a pre-Columbian house, the chief bent down in the central kitchen area, popped out a big hunk of pottery, and corroborated my sense that the daily life of the ancient society was much like today's. "You're right!" Afukaka exclaimed. "Look here, a pot support"—an *undagi*, as the Kuikuro call it, used to cook manioc.

These connections are what make the Xinguano sites so fascinating. They are among the few pre-Columbian settlements in the Amazon where archaeological evidence can be linked directly to present-day customs. Elsewhere, the indigenous culture was completely wiped out, or the archaeological record is spotty. The ancient

XINGU HISTORY

Radiocarbon dating indicates that people have lived in the Upper Xingu for at least 1,500 years.

6th century. The ancestors of today's inhabitants moved in from the west.

13th century. Groups organized themselves into integrated clusters with a regional population estimated at 30,000 to 50,000.

1542. Spanish conquistador Francisco de Orellana led the first European expedition down the Amazon, as chronicled by Gaspar de Carvajal.

18th century. Slave raids further decimated the Xinguano people.

1884. German anthropologist Karl von den Steinen visited the Xingu and estimated a population of 3,500.

1950s. Orlando, Cláudio and Leonardo Villas Boas led a campaign to found the Xingu reserve. The Xinguano population was about 500.

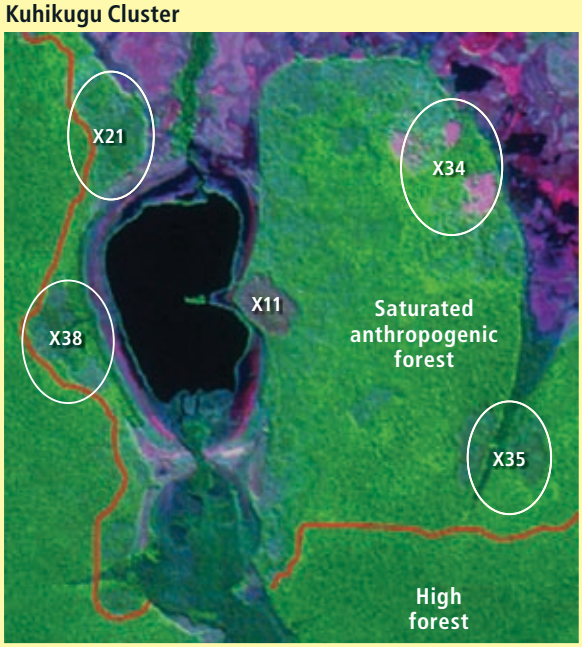
COURTESY OF U.S. GEOLOGICAL SURVEY/GODDARD SPACE FLIGHT CENTER/NASA/LANDSAT 7

[REMOTE SENSING]

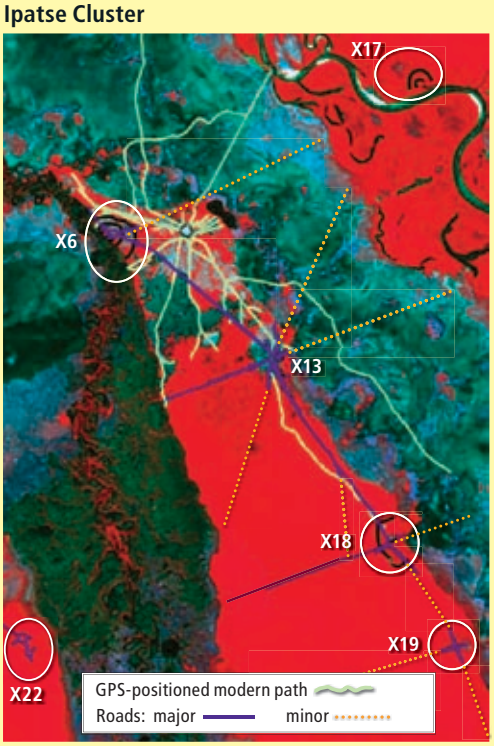
Peeking under the Canopy

Landsat satellite images, falsely colored to represent different infrared bands, show a mottled texture that indicates the forest has been shaped by humans, particularly in and around ancient settlements that the author and his team have identified in ground surveys. Forest in unmodified areas tends to look more uniform. Studies of soil properties and vegetation confirm that the region was once extensively cultivated.

Kuhikugu Cluster



Ipatse Cluster



At the present rate, the southern Amazon forest will be reduced to 20 percent of its original size over the next decade. Indigenous people are the stewards of the remaining biodiversity.

walled town I showed Afukaka was much like his current village, with its central plaza and radial roads, only it was 10 times larger.

From House to Polity

"Palatial" is not the word that usually comes to mind to describe a pole-and-thatch house. Most Westerners think "hut." But the house that the Kuikuro were building for the chief when I arrived in 1993 was massive: well over 1,000 square meters. It is hard to imagine that a house built like a giant, overturned basket without stone, mortar or nails could get any bigger. Even the average Xinguano house, at 250 square meters, is as big as the average American home.

What makes the chief's house stand out is not just size but also its position, located on the southern point of the central circular plaza. As one enters the village along the formal entry road, high-ranking families live to the right (south) and left (north). The arrangement reproduces, on a larger scale, the layout of an individual house, whose highest-ranking occupant hangs his hammock to the right, along the long axis of the house. The entry road runs approximately east-west; in the chief's house, his hammock is oriented in the same direction. When a chief dies, he is also laid to rest in a hammock with his head to the west.

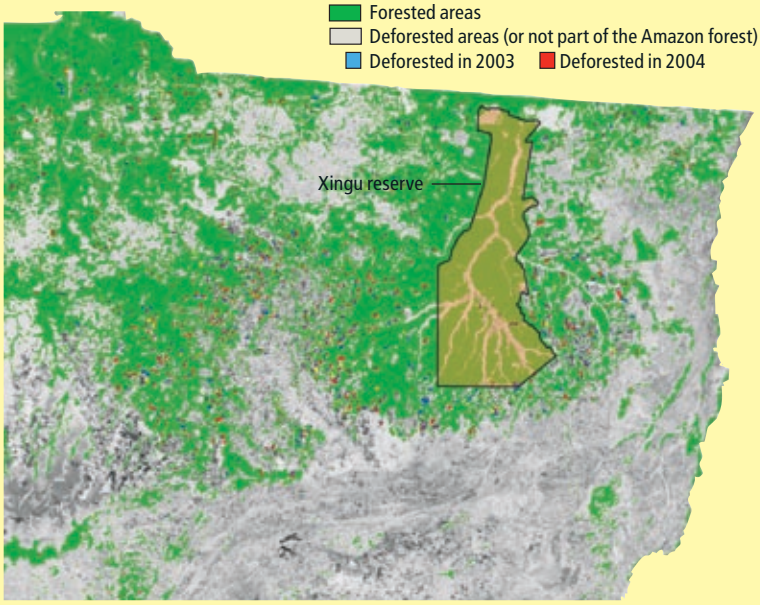
This basic corporeal calculus applies on all scales, from houses to the entire Upper Xingu basin. Ancient towns are distributed across the region and interconnected by a lattice of precisely aligned roads. When I first arrived in the area, it took weeks to map the ditches, plazas and roads using standard archaeological techniques. Beginning in 2002, we began using precise GPS, enabling us to map major earthworks in a matter of days. What we have found is an impressive degree of regional integration. The landscape planning seems almost overdetermined, with a specific place for everything. Yet it was based on the same basic principles of the current village. Main roads run east-west, secondary roads radiate out to the north and south, and smaller roads proliferate in other directions.

We mapped two hierarchical clusters of towns and villages in our study area [*see map on page 68*]. Each consists of a major ceremonial center and several large satellite towns in precise orien-

COURTESY OF MICHAEL J. HECKENBERGER (*map*); RICKEY ROGERS *Reuters/Corbis* (*aerial view*)

An Island of Trees

Indigenous lands have become the most important barrier to deforestation in many parts of the Amazon. The Xingu reserve was once deep in the tropical forest, but cleared landscapes of cattle ranches and soybean fields now impinge on it from all sides. For Xinguanos to provide for their growing population, do they, too, need to clear-cut the forest? The author's work suggests no. Their ancestors' model of land use, based on small towns and long agricultural rotation cycles, can support a substantially larger population.



DEFORESTATION in Mato Grosso is among the fastest in Brazil—in 2004 five hectares a minute.

tations relative to the center. These towns likely held 1,000 or more inhabitants. Smaller villages are located farther from the center. The northern cluster is centered on X13, which is not a town so much as a ritual center, rather like a fairground. Two large walled settlements lie equidistant to the north and south of X13, and two medium-size walled towns lie equidistant to the northeast and southwest. The southern cluster is slightly different. It is centered on X11, which is both a ritual center and a town, around which are medium- and small-size plaza settlements.

In land area, each cluster was more than 250 square kilometers, of which about a fifth was the built-up core area, making it roughly equivalent in size to a small modern city. Today most of the ancient landscape is overgrown, but forests in the core areas have distinctive concentrations of certain plants, animals, soils and archaeological artifacts, such as prolific ceramics. Land use was more intensive in the past, but the remains suggest that many practices were similar to those of the Kuikuro: manioc plots, small orchards of pequi fruit trees and fields of *sapé* grass, the preferred material for house thatch. The countryside was a patchy landscape interspersed with secondary forests that invaded fallow agricultural areas. Wetlands, which today are choked with Buriti palm, the most important industrial crop, preserve diverse evidence of fish farming, such as artificial ponds, raised causeways and weir footings. Outside the core areas was a more lightly populated green belt and even deeper forest wilderness between clusters. This forest, too, had its uses for animals, medicinal plants and certain trees, and it was considered the home of diverse forest spirits.

The areas in and around residential sites are marked by dark earth, which the Kuikuro call *egepe,* a highly fertile soil that has been enriched by household refuse and specialized soil-management activities, such as controlled burning of vegetation cover. People have altered soils the world over, making them darker, more loamy and richer in certain chemicals. In the Amazon these changes are particularly important for agriculture in many areas because the natural soil is so poor. In the Xingu, the dark earth is less prevalent than some areas, because local populations depend mostly on manioc and orchards, which do not require high-fertility soils.

Identification of large walled settlements over an area about the size of Vermont suggests that at least 15 clusters were spread across the Upper Xingu. But most of the region is unstudied, so the true number could have been much higher. Radiocarbon dating of our excavated sites suggests that ancestors of the Xinguanos settled the area, most likely from the west, and began to mold the forests and wetlands to their design about 1,500 years ago or before. In the centuries before Europeans first discovered the Americas, the communities were re-formed into hierarchical clusters. Records date back only to 1884, so the settlement patterns are our only way of estimating the pre-Columbian population; the scale of the clusters suggests a regional population many times larger than today, perhaps numbering 30,000 to 50,000.

Garden Cities of the Amazon

A century ago Ebenezer Howard's *Garden Cities of To-morrow* proposed a model for low-density, sustainable urban growth. A forerunner of today's green movement, Howard envisioned networked towns as an alternative to an industrial world filling with high-rise cities. Ten towns with tens of thousands of people, he suggested, could have the same functional and administrative capacity of a single megacity.

The ancient Xinguanos built such a system, a flat, green style of urbanism or proto-urbanism: an inchoate garden city. Perhaps Percy Fawcett was in the right place but looking for the wrong thing: stone cities. What the small-scale centers lacked in size and elaborate structures, they made up for in numbers and integration. Had Howard known of them, he might have devoted a passage to the "Garden Cities of Yesterday." The common conception of the city as a dense grid of masonry buildings dates to early desert oasis civilizations such as Mesopotamia but was uncharacteristic of many other environments. Not only the Amazon's tropical forests but also temperate forest landscapes throughout much of medieval Europe were dotted with towns and villages of similar size to those in the Xingu.

These insights are especially important today as the southern Amazon is redeveloped, this time by Western civilization. The transitional forest of the southern Amazon is being quickly converted into farmland and pasture. At the present rate, it will be reduced to 20 percent of its original size over the next decade. Much of what is left will be restricted to reserves, such as the Xingu, where indigenous people are the stewards of the remaining biodiversity. In these areas, saving tropical forests and protecting indigenous cultural heritage are, in many respects, one and the same thing. ■

MORE TO EXPLORE

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Boosting Vaccine POWER

Modern insights into the immune system have revived interest in adding ingredients that can supercharge old vaccines and make entirely new ones possible

By Nathalie Garçon and Michel Goldman

KEY CONCEPTS

- Vaccines are extremely effective at preventing disease, but they could work better, for more people and against a wider variety of illnesses.
- Advances in immunology have revealed how new classes of "adjuvants"—ingredients that stimulate immune responses to vaccines—can allow vaccine designers to target specific populations and pathogens.
- Novel adjuvants can make existing vaccines more effective and make previously impossible vaccines a reality.

—The Editors

The thought of birth defects caused by rubella, rows of iron lungs housing children crippled by polio, or the horrific sound of a baby struggling with whooping cough can still evoke dread among people who have seen firsthand the damage inflicted by these and other vaccine-preventable diseases. Fortunately, those scourges are virtually unknown to modern generations that have had access to vaccines all their lives.

For more than 200 years vaccines have proved to be one of the most successful, lifesaving and economical methods of preventing infectious disease, second only to the sanitization of water. Vaccines have spared millions of people from early death or crippling illnesses and made the global eradication of smallpox in 1979 possible. Health experts now pledge to eliminate polio, measles and perhaps one day even malaria—although, as we shall see, a malaria vaccine will require novel approaches to immunization to be successful.

Broadly speaking, the premise of vaccination is that exposure to a small sample of a disease-causing microorganism teaches the human immune system to recognize it and prepare to fight it off the next time it is encountered. But classical vaccines do not always work in all people, nor can they guard against all illnesses. Some populations, such as the elderly, may have immune systems too weak to respond sufficiently to traditional vaccines. And certain disease-causing organisms have been able to evade the kinds of immune defenses evoked by vaccines—malaria, tuberculosis and AIDS are examples of illnesses that vaccines still cannot reliably ward off. The principles of vaccination could also be extended to a host of other afflictions, such as cancer, allergy or Alzheimer's disease, but these applications would require provoking the immune system to respond to something it would normally recognize only weakly or not at all.

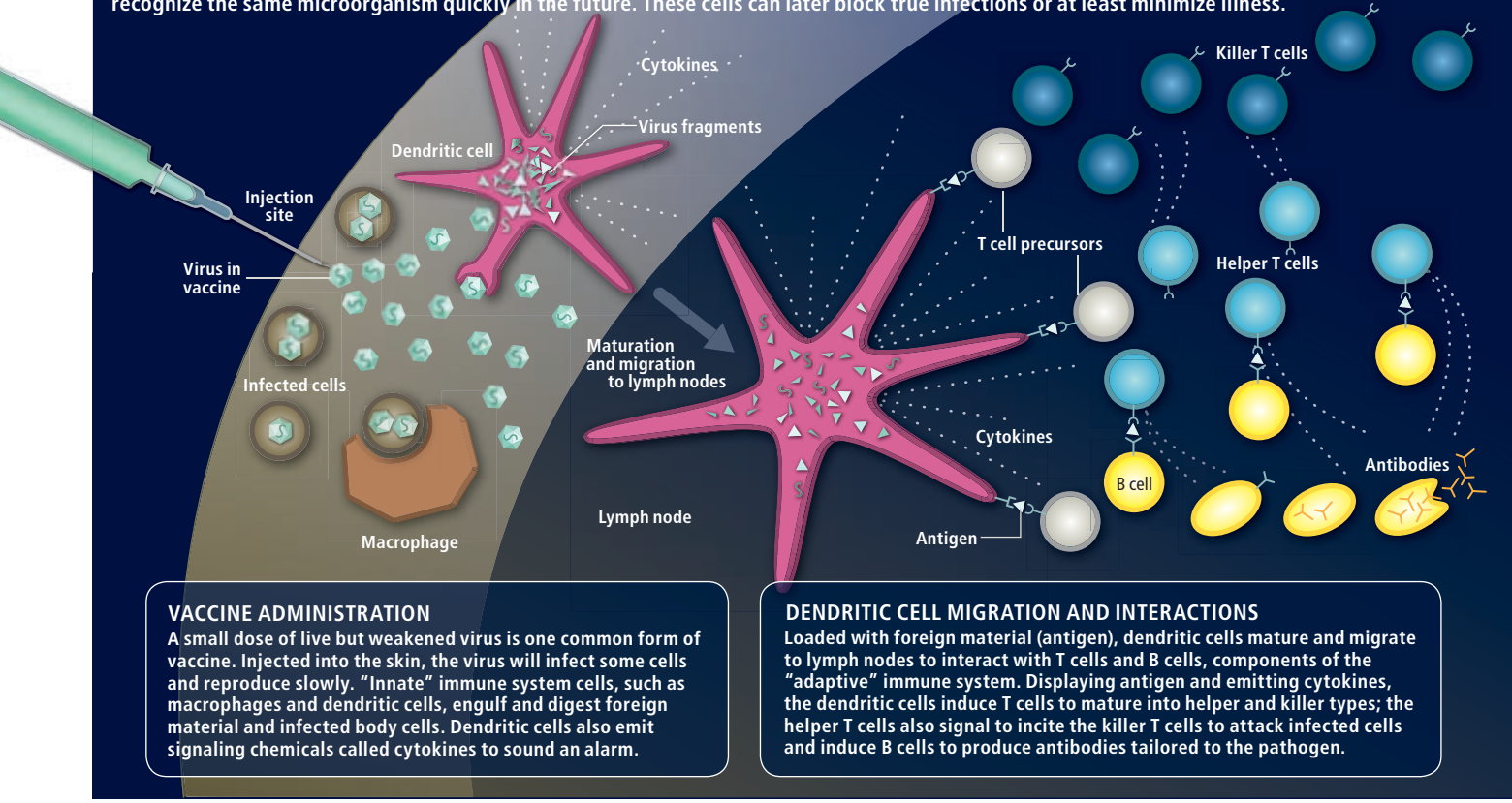
In all these situations, immune system stimulators that boost the body's ability to recognize and respond to a vaccine could make the difference. Such immunity-stimulating substances are often called adjuvants, from the Latin *adjuvare*, meaning "to help." Some have been known for more than a century and used to enhance vaccines and cancer therapies. Like the mechanisms underlying vaccines themselves, however, the ex-

AMY GUIP

[BASICS]

Vaccines Mimic Infection to Avert It

Vaccines deliver a killed or weakened pathogen, or pieces of it, to trigger an immune response that generates "memory" cells primed to recognize the same microorganism quickly in the future. These cells can later block true infections or at least minimize illness.



VACCINE ADMINISTRATION
A small dose of live but weakened virus is one common form of vaccine. Injected into the skin, the virus will infect some cells and reproduce slowly. "Innate" immune system cells, such as macrophages and dendritic cells, engulf and digest foreign material and infected body cells. Dendritic cells also emit signaling chemicals called cytokines to sound an alarm.

DENDRITIC CELL MIGRATION AND INTERACTIONS
Loaded with foreign material (antigen), dendritic cells mature and migrate to lymph nodes to interact with T cells and B cells, components of the "adaptive" immune system. Displaying antigen and emitting cytokines, the dendritic cells induce T cells to mature into helper and killer types; the helper T cells also signal to incite the killer T cells to attack infected cells and induce B cells to produce antibodies tailored to the pathogen.

act details of how adjuvants interact with immune cells were poorly understood until very recently. Tremendous advances in immunology, especially over the past decade, have provided new insights into how adjuvants produce their effects and opened avenues for designing vaccines tailored precisely to the population to be protected and the pathogen to protect against. With these new tools, vaccines that were once impossible to create are now in development, and existing vaccines are becoming more efficient and effective.

Mimicking Infection to Avert It

Many natural infections have at least one benefit in that a bout of illness confers lifelong immunity against the causative pathogen. An ideal vaccine would also offer such lasting protection, preferably with a single dose, and perhaps even protect against related threats, such as all members of the ever evolving family of human flu viruses. To achieve those goals, a vaccine must engage multiple cellular actors in the immune system, the same ones stimulated during a real infection.

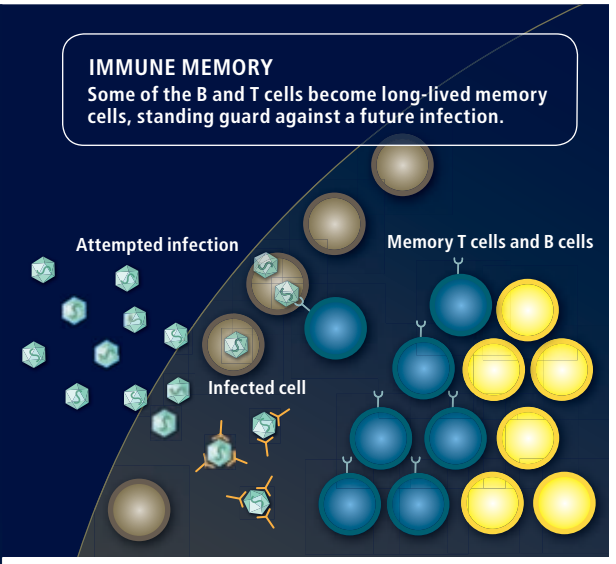
COMMON VACCINE TYPES

- **ATTENUATED:** Live but weakened whole virus or bacterium. Minimal reproduction extends immune cells' exposure to antigen without causing disease.
- **INACTIVATED:** Whole but "killed" and unable to reproduce or to cause disease.
- **SUBUNIT:** Fragments of the pathogen, such as genetic material or external proteins, provide antigen for immune cells to recognize.

When a wild pathogen enters the body for the first time, it immediately encounters cells of the innate immune system that are constantly patrolling for invaders. These sentries include macrophages and dendritic cells, which engulf and destroy pathogens as well as infected body cells. The guard cells then break down the material they have ingested and display samples of the intruder's components—known as antigens—so that members of the adaptive immune system, T and B cells, can become familiar with the pathogen's appearance. At the same time, the antigen-presenting cells release signaling chemicals called cytokines that induce inflammation and alert T and B cells to the emergency.

Once a population of T and B cells adapted to the specific pathogen matures, the B cells release antibody molecules, and killer T cells seek out and destroy cells that have already been colonized by the invader. It takes a few days for interactions with antigen-presenting cells to create these tailored T and B cells, but a subset of them can

MELISSA THOMAS (*illustrations*)



remain in the body as "memory" cells—sometimes for decades—ready to squelch any attempted reinfection by the same organism. Vaccines replicate this process by introducing a whole pathogen or fragments of it that will be recognized as a foreign invader. Not all vaccines succeed in generating a full immune response, but some pathogens can be stopped by antibodies alone, so killer T cells are not needed for protection.

The nature of the pathogen and how it causes illness are among vaccine designers' considerations when choosing what type of antigen to use. The material administered in a standard vaccine may be live but weakened ("attenuated") bacteria or viruses; killed or inactivated versions of the whole organism; or purified proteins derived from the original pathogen. Each choice has advantages and drawbacks.

Live attenuated vaccines reproduce very slowly in the body, but because they do reproduce and thus continue to present antigen to the immune system, they can trigger a robust and long-lasting immune response. Because of their inherently infectious nature, however, attenuated vaccines cannot be used in individuals with weakened immune systems, which may become overwhelmed. The danger of certain live viruses mutating and reverting to a virulent form also makes attenuated vaccines too dangerous to use for deadly pathogens such as HIV.

More common are vaccines consisting of whole virus particles that have been "killed" using a method such as heating. The particles cannot replicate, but the virus proteins are still relatively intact and easily recognized by immune cells, although periodic booster shots are required to reinforce the immune response.

A third form is the subunit vaccine, which presents antigen to the immune system without introducing microorganisms, whole or otherwise. This antigen can be isolated from the pathogen itself, or it may be manufactured through recombinant genetic engineering. Because subunit vaccines contain only part of the pathogen, however, they do not always trigger the danger signals required to stimulate the optimum immune response.

In recent years scientists have come to recognize the critical role played by antigen-presenting cells, particularly the dendritic cells, in assessing the level of threat posed by a pathogen and determining the necessary response. When dendritic cells become loaded with antigen at the site of infection or at the site of a vaccine injection, they mature and migrate to neighboring lymph nodes, where they begin the signaling and interactions that elicit protective B and T cell responses. Without the danger indicators unique to whole microorganisms, dendritic cells fail to mature and migrate properly, and subunit vaccines often require an adjuvant to provide the red flag that stimulates dendritic cells to action.

Most vaccines used in the U.S. already do contain one of the oldest adjuvants, alum, which is a shorthand term for members of a chemical family of aluminum salts. Although alum has been used in human vaccines since the 1930s and has proved its usefulness in many current vaccines, it is insufficient as a helper in vaccines against diseases that require more than antibody protection to be effective.

Various pathogens that can cause life-threatening infections such as HIV, hepatitis C virus, *Mycobacterium tuberculosis* and *Plasmodium* parasites (the source of malaria) can evade antibodies, and an effective vaccine against these pathogens would need to stimulate robust T cell responses. Indeed, efforts to fight these very challenging organisms spurred a revived interest in vaccine adjuvants while driving breakthroughs in understanding the immune system, which in turn has led to better adjuvants.

Adjuvant Revival

Even as French chemist Louis Pasteur was confronting a rabid bulldog to extract saliva for the first rabies vaccine in the 1880s, a New York bone surgeon was unwittingly inventing a technique for boosting overall immune response that can be considered the first use of adjuvants. Wil-

[THE AUTHORS]


Nathalie Garçon is head of the Global Adjuvant Center for Vaccines at GlaxoSmithKline Biologicals (GSKB), a vaccine manufacturer that has pioneered development of novel adjuvants over the past two decades. Garçon, a pharmaceutical scientist specializing in immunology, joined the company in 1990 to lead its adjuvant program. Michel Goldman is a professor of immunology at the Université Libre de Bruxelles in Belgium. His research into human immunity centers on factors controlling dendritic cells and Toll-like receptor signaling, which are crucial to the effectiveness of vaccines and vaccine adjuvants. Until September 2009, he also directed the Institute for Medical Immunology, funded in part by GSKB. He is now executive director of the Innovative Medicines Initiative, a European Commission partnership with the European Federation of Pharmaceutical Industries.

COURTESY OF GLAXOSMITHKLINE (*Garçon*); COURTESY OF MICHEL GOLDMAN (*Goldman*)

[VACCINE BOOSTERS]

Adjuvants Add Emphasis

Adjuvants enhance immune responses to vaccine antigens by several mechanisms, but their most potent effects are likely to be through activation of microbe-recognition receptors on dendritic cells. Depending on the type of threat they sense, dendritic cells will direct other immune cells to respond in different ways. Vaccine designers can use this knowledge to choose adjuvants that will not only boost immune response but also emphasize the desired responses.

liam B. Coley of the New York Cancer Hospital was intrigued by reports of tumors shrinking or disappearing entirely in cancer patients who became infected by a particular strain of *Streptococcus* bacteria, *S. pyogenes*. On the hunch that the patients' immune reactions to the bacteria were enhancing their ability to fight off the tumors, he began a series of experiments in 1881, administering the live bacteria and later infusions of killed bacteria to cancer patients. These treatments, which came to be known as "Coley's Toxins," achieved some impressive remissions, although exactly how they worked would long remain a mystery.

Early 20th-century researchers nonetheless extended the idea that bacteria and other substances could improve natural human immune responses. French veterinarian Gaston Ramon and English immunologist Alexander T. Glenny experimented with substances as varied as tapioca and aluminum hydroxide to boost the effectiveness of diphtheria and tetanus vaccines given to animals. During the 1930s other scientists found that suspending antigens in emulsions of oil and water could enhance vaccine potency, and bacterial extracts such as lipopolysaccharide (LPS), a component of some bacterial cell walls, continued to be explored. Many of these additives had the desired effects, but too often adverse reactions, such as excessive inflammation, made the approach unpredictable.

Interest in adjuvant research faded as a result, until the 1980s when the arrival of a new viral challenge called for every imaginable tactic to be deployed. HIV proved to be far beyond the reach of classical vaccination methods. The virus selectively attacked T cells, effectively disabling the adaptive immune system, and it morphed so continually that antibodies could never keep up with it. Vaccine researchers working with recombinant HIV proteins had to find ways to boost the immune system's recognition of the antigens, leading them to try combinations of known adjuvants as well as refining those to fashion new ones.

Perhaps the biggest breakthrough for adjuvant research came in 1997, however, with the discovery that specialized pattern-recognition receptors on and within dendritic cells are devoted to recognizing fundamental parts of microorganisms, such as the protein flagellin that is found in the tails of many different bacteria. These pathogen-detecting receptors provide the danger signal that spurs dendritic cells to action as well as information about what type of threat is present. Among these newly discovered cellular keys, a group known as the Toll-like receptors (TLRs) seemed most important for driving the dendritic cells' behavior [see "Immunity's Early-Warning System," by Luke A. J. O'Neill; Scientific American, January 2005].

To date, 10 functional Toll-like receptors have been identified, and each recognizes a different basic motif of viruses or bacteria. TLR-4 recognizes LPS, for instance, whereas TLR-7 registers the single-stranded RNA typical of some viruses. After these discoveries, it became clear that microbial extracts acted as immune-stimulating adjuvants because they provided a danger signal to dendritic cells via TLRs. The revelation of these mechanisms meant that a vaccine designer could use one or a combination of adjuvants to target specific TLRs.

Next-Generation Vaccines

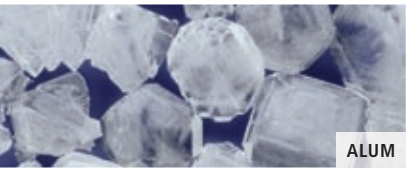
The research initiated in the 1980s and 1990s sought to identify and evaluate natural adjuvants, as well as synthetic or modified ones, that might be used to modulate the immune response to specific pathogens or in certain populations. These ingredients include the traditional adjuvants, such as alum, and oil-in-water emulsions, such as MF59 and AS03, both approved in Europe for use in certain influenza vaccines. More broadly, adjuvants can also be any chemical compounds that improve the quantity and quality of immune responses by acting on dendritic or other immune cell types.

Experimentation and advances in immunology have allowed scientists to eliminate elements that caused unwanted toxicity in earlier adjuvants and to mix and match adjuvant substances so that their collective action is optimized to elicit the desired immune response. One novel adjuvant, monophosphoryl lipid A (MPL), for exam-

ADJUVANTS OLD AND NEW

ADJUVANTS IN REGISTERED VACCINES

- Aluminum salts ("alum")
- Oil-in-water, water-in-oil emulsions
- Liposomes (lipid particles)
- Virosomes (lipids + viral proteins)
- Vitamin E
- Monophosphoryl lipid A (MPL), a purified derivative of bacterial lipopolysaccharide

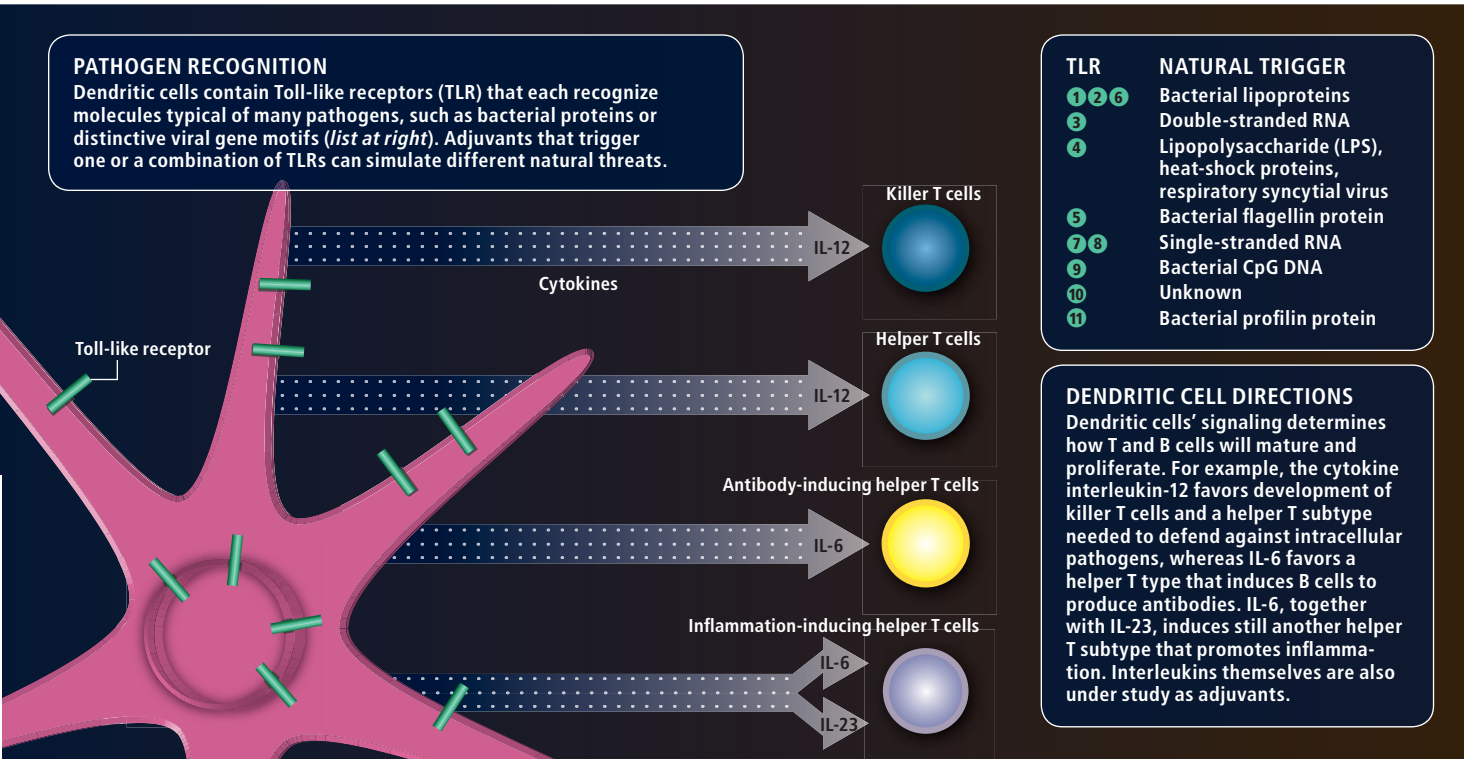


ALUM

ADJUVANTS IN DEVELOPMENT

- CpG, a bacterial DNA motif lacking methyl groups characteristic of human DNA
- Saponins (plant extracts):
  - QS21
  - Quil A
  - Immune-stimulating complexes (saponin + lipid cages)
- Viruses as antigen carriers:
  - Fowlpox
  - Vaccinia
  - Canarypox
- Viruslike particles, self-assembling viral shells containing no genetic material
- Interleukins and other cell-signaling molecules

ADAM HART-DAVIS *Photo Researchers, Inc.*



ple, was produced by detoxifying and further purifying one of the lipids from the LPS molecule, yielding an adjuvant with TLR-4-stimulating properties but without the unwanted toxicity. It has been incorporated into several vaccines that are already on the market or in late-stage clinical testing with encouraging results.

Among these is an experimental vaccine against malaria that one of us (Garçon) helped to develop as head of GlaxoSmithKline Biologicals's vaccine adjuvant center. Caused by protozoan parasites of the genus *Plasmodium*, malaria is a serious disease that kills more than a million people a year, mostly children under the age of five. These parasites are able to hide within cells, evading immune mechanisms. They also change form several times over the course of their life cycles, making it difficult to find an antigen that will serve as an effective vaccine target in all stages of infection. Eliciting both antibody- and T cell–mediated immunity to protect against these parasites by preventing them from entering cells and by destroying cells that are already infected is important. These goals, in turn, required adjuvants that go beyond alum.

Taking all these factors into account, our group developed a vaccine based on an antigen we call RTS,S, which joins a recombinant partial protein present on the parasite's surface before it enters the human host's blood cells and during early cell infection, and links it to a hepatitis B surface antigen to further stimulate immune recognition. This compound molecule is then administered with an adjuvant mixture consisting of an oil-in-water emulsion, MPL and QS21, a plant derivative used since the 1930s in veterinary medicine. After optimizing the formulation, we and our collaborators at the Walter Reed Army Institute of Research tried the vaccine in small human tests involving volunteers willing to stick their arms into a box of malaria-carrying mosquitoes and be bitten at least five times. Six out of seven vaccine recipients were protected from infection, whereas recipients of a version containing alum were not.

We tried the vaccine in small human tests involving volunteers willing to stick their arms into a box of malaria-carrying mosquitoes and be bitten at least five times.

Real-life conditions with continued exposure to the parasite are the ultimate test, and larger trials conducted in the Gambia among adults demonstrated 71 percent of recipients to be protected from infection during nine weeks of follow-up. Later trials in children in malaria-endemic areas of Mozambique showed that three doses protected 30 percent of the kids from infection, and the group's incidence of severe disease over six months was reduced by nearly 60 percent. An improved version of this vaccine containing liposomes is nearing the end of late-stage (phase 3) clinical testing in infants. As the first vaccine ever to show significant rates of protection against malaria infection and severe ill-

MELISSA THOMAS

ness, it fosters great hope for contributing to controlling the disease.

The success of this vaccine illustrates the potential for rational vaccine design combining antigen and adjuvants to produce the desired immune response—both in making new vaccines and in improving old ones. Many existing vaccines that are generally successful may not be safe or effective in certain parts of the population, including the people who need them most. Seasonal influenza is an example: the elderly and infants are most vulnerable to lethal flu infections because infant immune systems are not fully developed, and immune responses also decline with age. Only about half of people older than 65 who receive a standard flu vaccine will develop sufficient antibodies to prevent infection.

In contrast, an experimental seasonal influenza vaccine containing the oil-in-water emulsion AS03 yielded protective antibody levels in 90.5 percent of recipients 65 or older. Because adjuvants boost immune cell recognition of antigens, they can also be used to make effective vaccines with less antigen. This consideration becomes especially important in the case of a pandemic requiring a potentially huge population to be vaccinated quickly. Another experimental AS03 vaccine, this one against the avian H5N1 flu strain, elicited protective antibody responses using just a third the amount of antigen in a typical seasonal flu vaccine.

These examples illustrate the kinds of new vaccines that are close to widespread human use because the revival and development of adjuvants in the 1980s and 1990s are bearing fruit now. Scientists' realization during that era that the pattern-recognition abilities of dendritic cells are a critical link between the innate and adaptive immune systems has also permitted the design of new types of adjuvants. This work is in earlier stages but has the potential to create an arsenal of adjuvant components from which vaccine designers can pick and choose to build vaccines with unprecedented precision.

New Generation of Adjuvants

Along with advances in immunology and molecular biology, materials science has provided many new methods for achieving adjuvant effects. Liposomal carriers are already employed to encapsulate drugs and other substances, delivering their contents to a target tissue in the body while protecting them from degradation. When used to carry vaccine antigens, they offer similar protection, creating a depot that allows for extended exposure of the antigen to immune cells. Variations on this principle are seen in polymer antigen cages made, for example, both from natural polysaccharides, such as those found in bacterial cell walls, and from synthetic polyesters. These materials have the added benefit of incorporating natural or added immune-stimulating chemicals that can trigger desirable immune cell signaling.

PANDEMIC INFLUENZA requires large populations to be vaccinated. Adjuvants can make vaccines effective with less antigen per dose and possibly protective against flu strains that vary slightly from the original.

A variety of experimental cancer vaccines employing different adjuvant combinations have produced promising results.

As the language of immune cells has been deciphered, scientists have come to realize that the early signaling by dendritic cells to sound an alarm also directs the nature of the response depending on the type of threat at hand. Thus, a vaccine designer can theoretically tailor adjuvant combinations to summon an immune response that emphasizes antibody production or one that preferentially stimulates certain subsets of T cells. Indeed, signaling molecules themselves are among the substances being tried experimentally as adjuvants. A class of cytokines known as interleukins (IL) has long been used to enhance immunity in cancer and AIDS treatments, but interleukins are naturally produced by dendritic cells, and the cells' mixture of signals can determine which immune cells respond—for instance, IL-4, IL-5 and IL-6 enhance killer T cell production, whereas IL-2 and IL-12 will favor antibody responses.

Similar effects can be achieved through combinations of TLR activators. Various TLRs recognize microbial products, and one of them, TLR-4, also recognizes molecules released by the body under stress, known as heat-shock proteins. Some combinations of TLR activators with non-TLR adjuvants, such as oil emulsions, show particularly strong synergy in activating dendritic cells and may prove useful in some of the most challenging vaccine applications.

Among these is cancer, an unusual vaccine

ANTONIO SCORZA Getty Images

target because instead of being a foreign invader, cancer cells arise from the victim's own body. As a result, the immune system does mount some response to tumor cells, but it is rarely adequate to fight off the cancer. Attempts to create therapeutic vaccines to stimulate an immune reaction to tumor cells have met with disappointing results; however, the right combination of adjuvants may make a difference. A variety of experimental cancer vaccines employing different adjuvant combinations have produced promising results.

One of these, now in late-stage clinical trials, combines an antigen (Mage-A3) that is highly specific to certain tumor cells with AS15, an adjuvant mixture of stable liposomes, MPL and QS-21, as well as a bacterial component called CpG. In trials among patients with non-small-cell lung cancer, 96 percent of those receiving the vaccine showed a strong Mage-A3 antibody response and indications that desirable interleukin signaling had been triggered. Almost a third experienced stabilization or regression of their tumors. Another current trial is deploying CpG along with chemotherapy and radiation therapy against several types of cancer. CpG is a distinctive bacterial DNA motif that is recognized by TLR-9 and spurs dendritic cell activation of strong T cell responses. Thus, its use as an adjuvant echoes William Coley's long-ago bacterial treatments for cancer patients. Fittingly, the company created to develop CpG as an adjuvant was named Coley Pharmaceuticals.

The various adjuvant systems we have described are pushing the limits of disease prevention through vaccination and bringing great hope in areas of unmet medical need. Early clinical tests of CpG added to ragweed antigen have shown promise as a vaccine against hay fever. Adjuvants' ability to induce immune defenses that recognize related strains of flu offers the possibility of creating more broadly protective flu vaccines. And for the first time, people whose immune systems are compromised by disease or chemotherapy may have access to vaccines that are able to evoke immune protection. Adjuvants may not be the answer to all the shortcomings of the modern vaccine arsenal, but they will surely provide part of the solution.

Modulating the immune system is delicate work, of course, and an ongoing critical assessment of vaccine safety and transparent dissemination of accurate information about next-generation vaccines and adjuvants is essential. A detailed understanding of the mode of action of the adjuvants incorporated into new vaccines is guiding their development and will direct their use and monitoring. Encouragingly, the most advanced adjuvanted preventive vaccines have not shown any signs of problems that warrant concern, but developers must remain vigilant.

As this field continues to progress, vaccines will better serve specific subpopulations and target diseases in a rational manner that elicits the optimum immune protection, while balancing safety and efficacy. This is vaccine development of the future. And that future is nearly here. ■

MORE TO EXPLORE

Deciphering Immunology's Dirty Secret: Can Innate Immune Adjuvants Save Vaccinology? Kate Travis in *The Scientist,* Vol. 21, Issue 1, pages 46–51; January 2007.

GlaxoSmithKline Adjuvant Systems in Vaccines: Concepts, Achievements and Perspectives. Nathalie Garçon et al. in *Expert Reviews of Vaccines,* Vol. 6, No. 5, pages 723–739; October 2007.

Vaccine Adjuvants: Current Challenges and Future Approaches. Jennifer H. Wilson-Welder et al. in *Journal of Pharmaceutical Sciences,* Vol. 98, No. 4, pages 1278–1316; April 2009.

[IN THE WORKS]

Next-Generation Vaccines

The vaccines below incorporate novel adjuvants and are approved in some countries or are in late-stage (phase 3) human testing.

DISEASE	VACCINE	ADJUVANT COMPONENTS	DEVELOPMENT STAGE	COMPANY
Hepatitis A	Epaxal	Virosomes	Approved in Europe	Crucell
Hepatitis B	Fendrix	AS04 (alum, MPL)	Approved in Europe	GlaxoSmithKline (GSK)
	Supervax	Synthetic MPL RC-529	Approved in Argentina	Dynavax Technologies
	Heplisav	CpG	Phase 3	Dynavax Technologies
Human papillomavirus	Cervarix	AS04	Approved in 96 countries	GSK
Influenza (seasonal and pandemic)	Fluad, Focetria	MF59 (oil-in-water emulsion)	Approved in Europe	Novartis
	Inflexal V	Virosomes	Approved in Europe	Crucell
	Prepandrix, Pandemrix	AS03 (oil-in-water, vitamin E)	Approved in Europe	GSK
	Seasonal elderly vaccine	AS03	Phase 3	GSK
Malaria	Mosquirix	AS01 (liposomes, MPL, QS21)	Phase 3	GSK
Non-small-cell lung cancer	Mage 3 vaccine	AS15 (liposomes, MPL, QS21, CpG)	Phase 3	GSK
	CimaVax EGF	Montanide ISA-51 (oil-in-water)	Approved in Cuba and Chile	Bioven

Privacy AND THE Quantum Internet

Courtesy of some of the weirdest laws of physics, we may someday be able to search and surf the Web without anyone collecting our data > BY SETH LLOYD

KEY CONCEPTS

- Current Web searches, even when anonymized, can still reveal personal information about the user.
- Over a quantum version of the Internet now being developed, search engines could return queries back to the users with the answers—and with the assurance that no one has saved or copied the data.
- Quantum searches will require search engine databases to use a new kind of memory storage, which is already being demonstrated in the laboratory.

—The Editors

Privacy is hard to come by these days, particularly on the Internet, where every time you Google something your desires are recorded for posterity—or at any rate, for advertisers.

Internet search companies say they protect their clients' privacy by encrypting personal information and by using numbers instead of names to give their users anonymity. The problem is that anonymization is not always effective. AOL user number 4417749 found this out the hard way in 2006 when AOL decided to publish online a list of 20 million Web searches, including hers and those of 657,000 other users. Reporters were able to track down the 62-year-old widow in Lilburn, Ga., by analyzing the content of her searches. Luckily, Thelma Arnold was relatively unembarrassed by the revelation of her identity and intimate interests. How many of us could say the same?

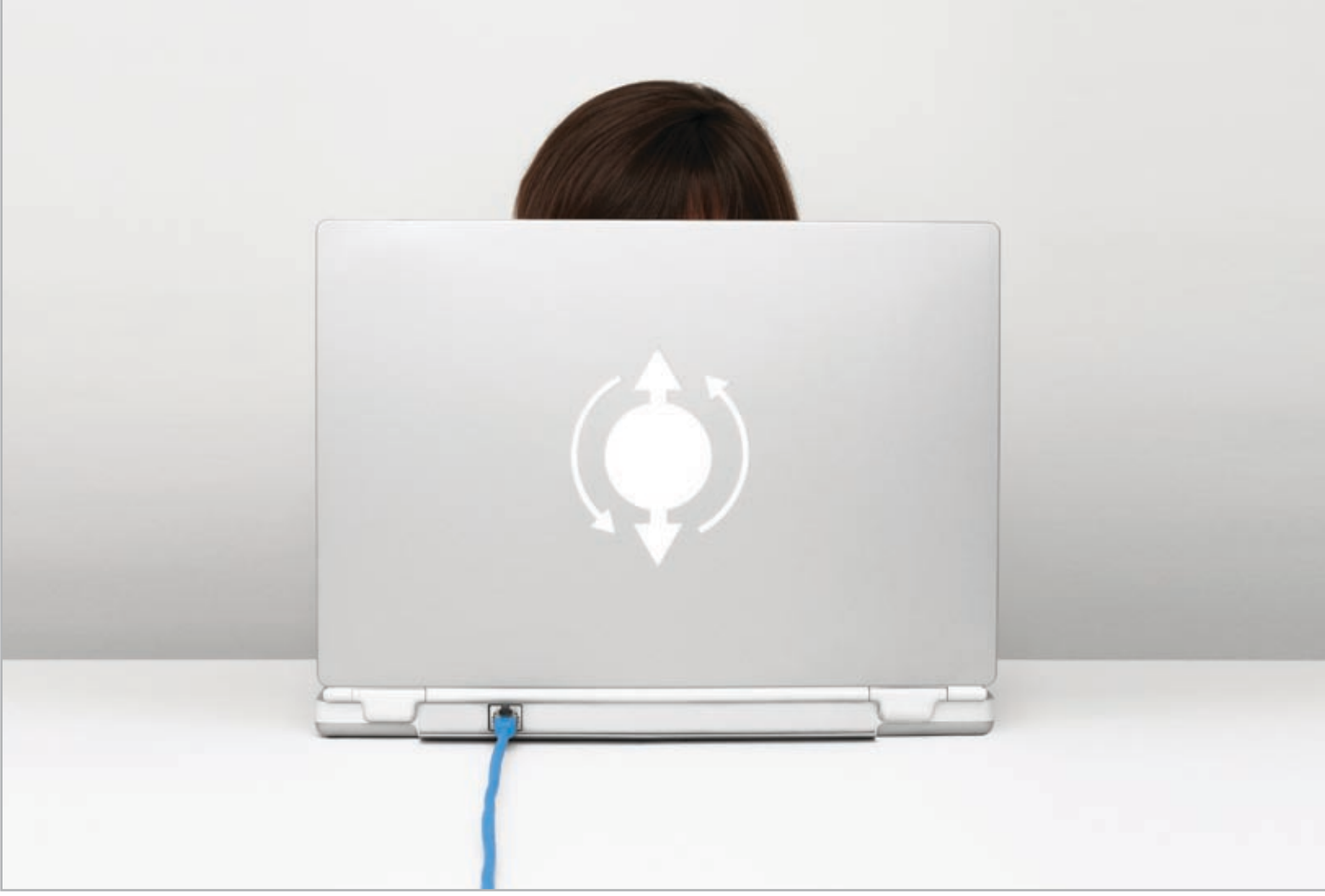
The laws of physics, however, could come to the rescue. Communication over special "quantum channels" already enables banks and other institutions to send data with virtually unbreakable encryption. Thus, the technology already exists to hide your searches from eavesdroppers who might intercept your queries. But in the future a new "quantum" version of the Internet may enable you to send queries and receive answers with the assurance that no one—not even Google—knows what questions you have asked. Moreover, the same technologies that will guarantee private searching could also guarantee privacy during the entire online experience.

Of course, search engines save and analyze users' data so that they can display targeted ads. That is how they cover their expenses and make a profit. If they decide to keep the users' data private, the search engines will need a new business model. And users may have to decide if they are willing to pay for searching or if they would rather do it free and give their searches away.

Nonclassical Listeners

It was with some sense of misplacement that in the spring of 2004 I found myself attending a billionaires' banquet during a conference in Monterey, Calif. My role, as near as I could make out, was to be the guy who jumps out of the cake—in other words, to entertain guests interested in quantum technology. The legitimate billionaires at the event included Sergey Brin and Larry Page, the founders of Google. To my surprise, Brin and Page knew a lot about quantum information. After some wild speculation on how quantum physics might change the way people interact with the Internet, I suggested that I would work with my colleagues to investigate "quantum Internet search," whatever that might prove to be.

The ability of quantum physics to supply complete privacy stems from a simple fact: systems in the quantum realm (which includes anything from elementary particles to molecules)



MICROZOA Getty Images; SCIENTIFIC AMERICAN (*graphic on computer*)

can exist in multiple states. At any particular time, an atom can be in several different places; a particle of light, or photon, can be polarized both vertically and horizontally; an electron's magnetic moment can point up and down, and so on. As a consequence, whereas classical (as opposed to quantum) data bits register either the value 0 or the value 1, quantum bits can register 0 and 1 at the same time. Also, whenever a quantum bit takes on the values 0 and 1 simultaneously, you cannot make an exact copy of that quantum bit, and any attempt to do so will change the state of the bit. This rule, known as the no-cloning theorem, also applies to strings of quantum bits, which, for example, can represent words or sentences. As a consequence, someone eavesdropping on a quantum channel—typically an optical fiber carrying photons in multiple polarization states—will not be able to "listen" to the communication without disturbing it, thus revealing the intrusion.

Several different quantum encryption techniques exist to exchange data in complete privacy thanks to no cloning. Yet such techniques presume that the addressees be allowed to read the data you sent them: merely sending Google an encrypted search query would not help. Last year, however, my colleagues Vittorio Giovannetti of the Scuola Normale Superiore di Pisa in Italy and Lorenzo Maccone of the University of Pavia in Italy and I discovered that the no-cloning theorem also makes private queries possible. In the protocol we devised, a user must be able to send the search engine a "quantum question"—a string of quantum bits that simultaneously contains the true question and another one. (It does not matter what the second question is: your computer could even supply a random one automatically.)

The search engine searches its database for the answers to your multiple questions and combines questions and answers into a new quantum package, which it sends back to you. If the search engine makes a copy of the questions for its records, you will be able to tell that your privacy was violated because the quantum state of your original questions will be perturbed in a way that your computer can detect. Crucially, the search engine can provide answers without physically detecting (let alone cloning) the string of bits that encodes the questions and thus without knowing what the questions were.

Although such magic is impossible with current computers, databases and networking

BROAD NEW APPLICATIONS

A future quantum Internet could enable users to interact in ways that are just not possible with current technology.

In a multicandidate election, **quantum voting** (in which voters express all preferences between any possible pairing of candidates) will favor the candidate who satisfies the maximum number of voters.

Similarly, **quantum auctions** will maximize the number of users who get to buy what they want for a fair price.

Future quantum computers will download disposable **quantum software** able to solve certain problems exponentially faster than ordinary software ever could.

In the distant future, a quantum Internet might even enable the **teleportation** of physical objects.

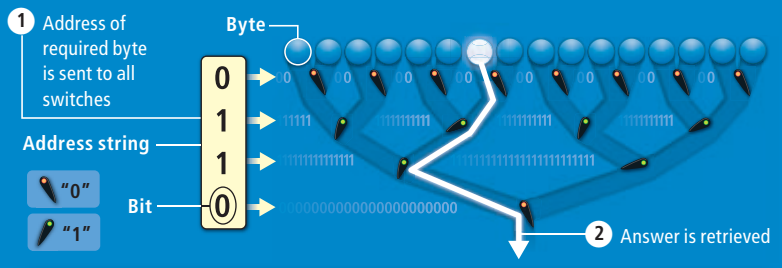
[MEMORY FOR QUANTUM SEARCH ENGINES]

Pssst! Keep This to Yourself

To offer absolute privacy, search engines will have to store information about the Web's content in a system called a quantum RAM. Users will send multiple queries as a single "quantum package." Quantum RAM will add the answers to the package and return it. Any disturbances in the package's quantum state will alert the user to privacy violations. Quantum RAM will require an architecture called bucket brigade in place of ordinary RAM architecture.

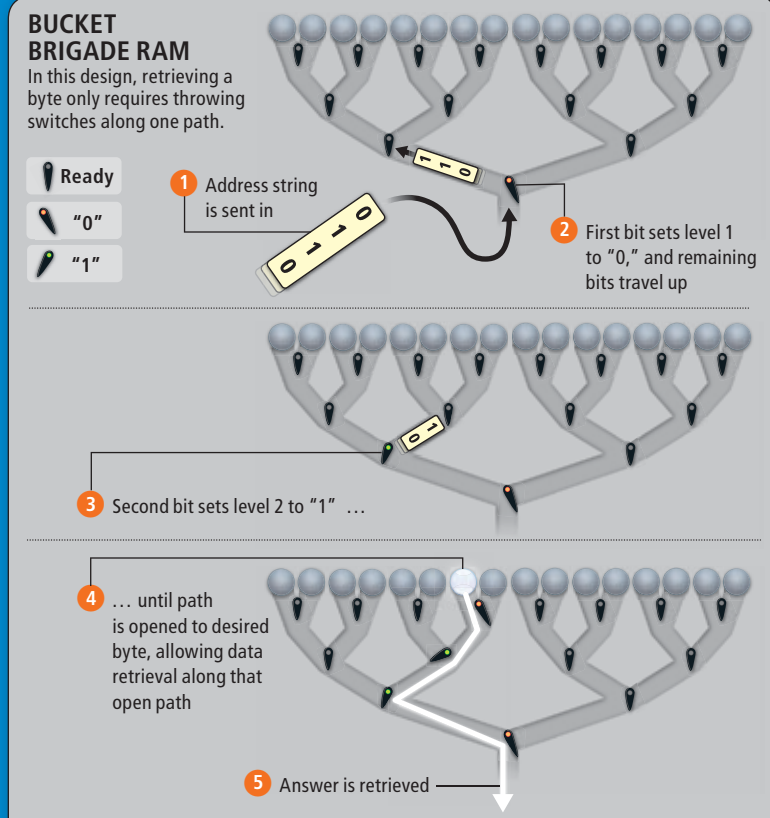
ORDINARY RAM

Data bytes are arranged in a treelike array. Retrieving a single byte involves throwing all switches in the array. For a quantum RAM, throwing a large number of switches would be impractical: because of the fragility of quantum states, the error rate would be too high.



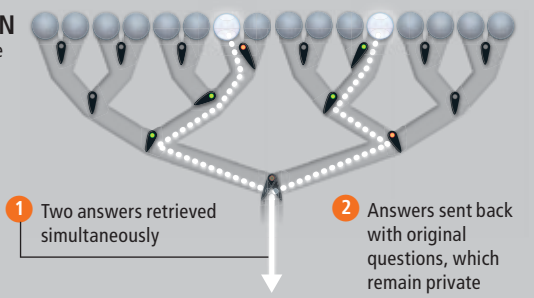
BUCKET BRIGADE RAM

In this design, retrieving a byte only requires throwing switches along one path.



QUANTUM VERSION

In quantum bucket brigade RAM, two paths can be opened to retrieve two pieces of data so they can be sent back with the original questions.



hardware, we realized that it is not technologically out of reach. The first requirement for quantum private queries is a rudimentary quantum Internet. The technology to exchange quantum messages along a dedicated line already exists and is in use for secure communication. A full-fledged quantum Internet, however, will have to be not just a line between two points but a network whose nodes route data packets so that any user can reach any other user or any Web server. It turns out that routing data without making temporary copies of them—and thus without suffering the consequences of the no-cloning theorem—is a nontrivial task and requires a sophisticated technology now at the experimental stage, called a quantum router. A prototype of such a network may become available within five to 10 years.

The second requirement for private Web searching is that users and data servers possess rudimentary quantum computers, meaning computers that are able to store and handle quantum bits. Unfortunately, quantum bits are notoriously fickle and tend to spontaneously lose their multiple quantum states within a fraction of a second. Experimental quantum computers that store quantum bits in the magnetic states of single ions suspended in a vacuum, for example, can store only eight bits or so at a time so far. A full-fledged quantum computer would require hundreds if not thousands of quantum bits and is probably many decades away, even as a laboratory demonstration. Fortunately, though, for the purpose of quantum private searches, only 30 quantum bits or so will be sufficient: if properly coded, a 30-bit query can pull an answer out of a database with more than a billion entries. Such 30-bit "quantum microprocessors" might also become available in five to 10 years.

Not So Random

So far everything looks good: quantum private searches seem to require only very simple quantum computers and quantum communication systems. Now the hard part comes. To answer a user's multipronged quantum question, a search engine's database must be able to supply the answer to each component of the question simultaneously. Doing so will require a new type of data storage called quantum random-access memory, or quantum RAM.

RAM is just a device for storing data, arranged in a treelike structure. Each piece of data is a sequence of eight bits, or a byte, and has an address that is itself a sequence of bits. Bytes are

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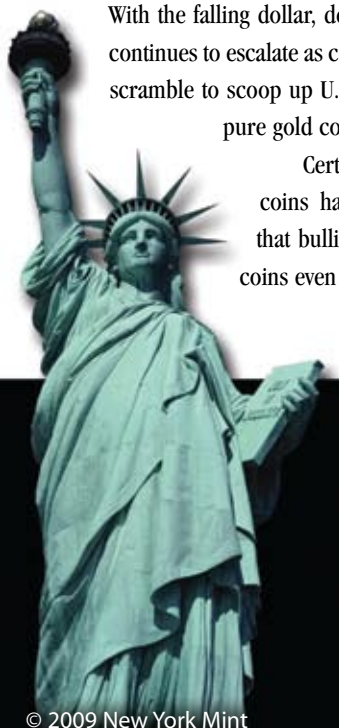

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like the leaves on the tree; the address controls the route from the trunk to the particular leaf. The first bit of the address specifies which of two branches to take at the lowest level of the tree, the second bit controls the second-level branching, and so on. The branches double at each level, and in a traditional RAM with 30-bit addresses, retrieving data requires throwing 2^{30} (more than one billion) switches.

One could design a quantum version of traditional RAM. The only difference is that the switches that route information through the binary tree must now be capable of routing information through two different branches simultaneously, because each bit of a quantum question can specify two different routes. Such quantum switches can be built using existing technology, such as semitransparent mirrors that "split" photons making them follow two different paths at once. The problem is that quantum circuits are exquisitely sensitive to noise and errors: if just one of the switches is messed up, the privacy of the corresponding bit is lost. Because a typical address bit controls a huge number of switches, the chances of losing privacy are very high.

Giovannetti, Maccone and I came up with a different design for addressing RAM (both quantum and classical), in which far fewer switches are thrown for each memory call. The secret is to route address bits along the same tree branches that data are to follow, rather than through separate addressing lines. Because the address bits are passed sequentially through the array, we call this a "bucket brigade" RAM [*see box on opposite page*].

The bucket brigade architecture requires throwing just one switch at each level of the array, whereas conventional RAM throws every switch at every level. The savings are striking: a bucket brigade RAM with a billion memory slots throws 30 switches for each memory call, compared with a billion switches thrown for each memory call in conventional RAM. And the benefits of the bucket brigade architecture, in terms of both error rate and energy savings, grow exponentially with the number of bits.

The Solace of Quantum

At first, we thought the bucket brigade idea had the potential to revolutionize the industry of classical RAM, and visions of dollar signs began to dance through our heads. But we soon found out that others had thought of a similar design before and that anyway the design was too slow for classical RAM (although it could be an energy-saving solution for nonvolatile memories such as those used in digital cameras).

But the bucket brigade design would be crucial for quantum searches, because its architecture can tolerate an error rate of one in 30, rather than one in a billion. The memory medium for a quantum RAM could consist of a conventional physical support. For example, the data could be stored in billions of tiny mirrors like those that make up the surface of a conventional CD. The truly quantum part of the quantum RAM is the switching array, which could be constructed from switches that each can shunt quantum bits along both branches at the same time. Such quantum switches already exist and attain error rates sufficiently low to build a quantum RAM with a billion slots or more.

Of course, assembling quantum switches to make a large quantum RAM will likely prove to be hard, not to mention the problem of connecting quantum RAM to quantum communication channels to implement quantum private queries. But none of the difficulties seem insurmountable. Incidentally, we realized recently that the data-routing techniques of our quantum RAM design could be applied to switching networks of the quantum Internet as a whole. People could surf the Web in complete anonymity, without revealing not only what they are searching for but also what Web sites they are visiting.

A few months after my colleagues and I had nailed down the details of how to build quantum RAM and make quantum private queries, I ran into Brin and Page at a conference in Napa, Calif. In a hot tub beneath fig trees, as the stars wheeled overhead, I described how quantum queries worked and what their benefits might be. Their first response was that Google's business model was to keep the information about all queries and to use it to prioritize advertising and future search results. Not retaining the information about queries had not occurred to them. When I put to them the evident advantages of a new, quantum business model—based on charging customers for search results—they thought some more. "Okay," they said, "Let's see if you can build it."

Recently Francesco De Martini and his group at the University of Rome "La Sapienza" have done just that. Using lasers, polarizers and photon detectors, they built a simple quantum RAM and demonstrated our search protocol on a small database. Quantum private queries are thus a real possibility. If someday we will have larger quantum RAMs or a viable quantum Internet, what happens then is anybody's guess. ■

[THE AUTHOR]

Seth Lloyd is professor of mechanical engineering (or a "quantum mechanic," as he likes to describe himself) at the Massachusetts Institute of Technology and director of M.I.T.'s W. M. Keck Center for Extreme Quantum Information Theory. He developed one of the first theoretical models for quantum computation and is working with several groups to construct quantum computers and quantum communications systems. Lloyd's book *Programming the Universe* was published by Knopf in 2004.

MORE TO EXPLORE

Best-Kept Secrets. Gary Stix in *Scientific American,* Vol. 292, No. 1, pages 79–83; January 2005.

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Biotech's Plans to Sustain Agriculture

Popular movements may call for more organic methods, but the agricultural industry sees biotechnology as a crucial part of farming's future

KEY CONCEPTS

- By 2050 or so, agriculture will need to produce about 50 percent more food than it currently does because of the expanding population. Traditional crops and farming methods could not sustain that much productivity.
- Representatives from the agricultural industry defend genetically modified crops as one of several tools that should be used to help farmers in developing countries become more productive.

—The Editors

If environmental and economic sustainability is ultimately a matter of balancing the human race's consumption and productivity, then the agricultural industry leans heavily on both sides of that scale. Its drain on the earth's resources is enormous: it claims 70 percent of all freshwater taken by our species and more than 40 percent of the planet's solid surface (nearly all the arable land), with attendant casualties in biodiversity. Yet modern agriculture is also the only reason we can produce enough food to nourish our population of 6.8 billion—a number slated to reach more than nine billion by midcentury. Keeping up with that steeply rising demand thus defines the challenge of sustainability not only for agriculture but for humanity.

Agriculture depends on many technologies, but biotechnology might be the most influential among them. To find out how the industry perceives its prospects for raising both global crop productivity and sustainability, contributing editor John Rennie spoke with representatives of four leading agricultural biotechnology companies. What follows here is an abridged version of their edited conversation.

—The Editors

THE PARTICIPANTS

James C. Borel
Group Vice President, DuPont

Valdemar Fischer
President, Syngenta Crop Protection, North America

David A. Fischhoff
Vice President, Technology Strategy & Development, Monsanto

Antonio Galindez
Vice President, Crop Global Business Unit, Dow AgroSciences

COURTESY OF DUPONT (*Borel*); COURTESY OF SYNGENTA (*Fischer*); COURTESY OF MONSANTO (*Fischhoff*); COURTESY OF DOW AGROSCIENCES (*Galindez*)

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SCIENTIFIC AMERICAN: How much of industry's effort to make farming and agricultural biotechnology sustainable represents a response to a demand in the marketplace for sustainability today, as opposed to a sense that there will be a future market opportunity or imperative for it?

BOREL: Sustainability is something that's core to DuPont and has been for a couple of hundred years. And biotechnology is one of the tools that we employ to help us move forward. As I think about agriculture, biotechnology is helping us help farmers produce more on the same or fewer acres of ground in more sustainable ways. I think about biotechnology as a set of tools, and they are helping us live out the mission of the company.

FISCHHOFF: It's been one of the goals of agricultural biotechnology all along to produce more with less, to reduce pesticide inputs, to deal with issues such as insufficient water or drought tolerance. Increasing population, increasing food demand and issues such as climate change have only redoubled our focus on those things.

GALINDEZ: You have to also take into account that as an industry we need to forecast the market environment, the regulatory environment, the environmental standards 10 or 15 years down the road, because every product we discover today takes that long to launch to the market. You always know that those standards continue to increase, and they have done so for the past 50 years. So I think as an industry, it has always been there in the fabric of the way we work.

FISCHER: With the challenges that we have going forward—with a growing world population and changes in diet—we know that in 25 or 30 years we are going to have to produce 50 percent more food than we are producing today. So we will have to grow more from less. It is our view at Syngenta that biotechnology is one of the tools to achieve that goal. To manage this challenge, growers will need to have access to the best available technology.

SA: Major conservation and sustainability worries involve freshwater and topsoil. What are some of the best technological options for tack-

NEW STRAINS of crops with desirable traits are under development using a variety of transgenic and breeding technologies. Public controversies over the plants' environmental and economic effects persist, however.

ADAM GAULT *Photo Researchers, Inc.*

ling these problems? Perhaps we can talk about nontechnological options, too.

FISCHHOFF: For agriculture, the world is divided into those crops that currently get sufficient freshwater from sources such as rainfall and those for which farmers need to resort to harvesting water, say, through irrigation or from other sources. But I think even in cases where crops are primarily rain fed, you could argue that nearly every crop at some point during its growing season has less than optimal water. The ways of addressing that big challenge, both at Monsanto and industrywide, are really mainstays of what we do in agriculture these days.

One is through breeding—by adapting crops as best we can and using the natural diversity in the crop germplasm to increase the levels of drought tolerance, which is the capability to better use the water that is available. And over and above that, there is enhancing that capability using genetic engineering techniques—to bring new genes into crops and give them greater tolerance to drought-like conditions. I think both those techniques are showing excellent promise. This has been a long-standing problem in agriculture and for agricultural biotechnology, and I think we're finally seeing the day when we can look forward to crops that have a much better water-utilization efficiency.

BOREL: Drought tolerance and nitrogen-use efficiency are very exciting. They're not going to be ready next year, but they're not very far away, either. If you think about the broader issues that you mentioned, often times the solution is a suite of technologies or maybe even something beyond technology involving management practices. For instance, farmers have moved toward significant reductions in tillage, which has helped reduce soil erosion and reduced farming's environmental impact—this has been partly enabled by advances in crop genetics, partly by better crop-protection chemistries, partly by better equipment, and so on. So the whole system is moving forward, and most times you find farmers are as interested or even more interested in environmental sustainability than the folks who don't live on the farm.

FISCHER: In the case of Syngenta, we have programs that identify genetic variation and physiological changes in plants that help them to survive drought and other stress conditions, and we try to incorporate those genes identified through breeding technology. We expect to launch our first water-optimized products after 2011. We also are developing other alternatives. Take the product that we are introducing next year here in the U.S. called Invinsa. It protects crop yields during extended periods of high temperature and mild to moderate drought and other crop stresses.

FISCHHOFF: The general public may not realize that in some cases the benefits of modern agriculture technology come from the dissemination and adoption of conservation tillage and reduced tillage methods. And those in turn have been largely helped—not solely but largely—by the use of herbicide-tolerant crops, like those with our Roundup Ready trait and others, which help farmers use low-tillage methods much more effectively. It's not the only reason why herbicide-tolerance technology is a good thing and helps farmers and helps sustainability, but it's one of those side benefits that I think doesn't get mentioned often enough.

GALINDEZ: I think all the companies here today are going to have significant investments addressing drought and flood or excessive water or reductions in nitrogen fertilizer use. But there are other angles. For example, we are benefiting from biotechnology today in the area of healthy oils. If you look just at the program Dow AgroSciences has with omega-9 fatty acids, then you know we have removed, in the past three years, half a billion pounds of trans fats and saturated fats from the North American diet. Think about

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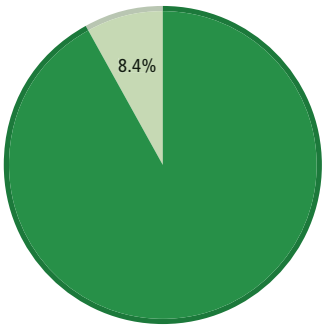

GENETICALLY MODIFIED crops make up a small but rising share of farm productivity, as reflected in the amount of arable land bearing them.

the secondary impact of those health indications in the whole environment; that's another aspect that people are not normally aware of, of what modern agriculture is bringing to the table.

SA: Are there nonbiological aids to sustainability that you in the biotech industry are counting on to emerge? For example, I've heard hopeful discussion about improvements in irrigation technologies and ways of using information technology to deliver water more prudently to crops. To what extent are you in biotech depending on complementary technologies in other industries and their timelines for development?

FISCHHOFF: All those technologies really go hand in hand. We've made a commitment at Monsanto to work toward doubling the yields in the major crops that we work on—in corn, soybean and cotton, in particular—by 2030. And we see that result as having to come from three different types of effort. One is clearly biotechnology in the sense of new gene insertion and new traits. The second is biotechnology in the support of breeding—basically, DNA-marker-assisted breeding to enhance and improve the rate of yield increase available to plant breeders. And then the third is this whole area of agronomic practices, which includes precision agriculture based on remote sensing and global positioning. That is, planting the right seed in the right place depending on the field conditions or having the precise application of pesticides, nitrogen fertilizer or other inputs. It takes advantage of new equipment for irrigation and new planting technology, for example, that would allow putting more plants per acre while still getting high yields. I don't think any one of those pieces alone will allow us to achieve these goals. I think we really need all three working together.

SA: Transgenic technologies are the ones most synonymous for the public with the development of many of the traits you mentioned.

FISCHER: At Syngenta, we believe that the combination of different technologies is actually what is going to allow us to increase food production by 50 percent over the next 25 years, which is what we need to do to feed the growing world population. So it's not only biotechnology; it's not only seed genetics; it's also crop-protection chemicals and the technologies associated with their use. Of course, we know that genetically modified foods and pesticide products are the most extensively tested and regulated in the entire food sector, so that should give us confidence that when these products come to the market they are tested and they are safe if they are used according to the labels.

FISCHHOFF: There is still a lot of debate, at least in some sectors. I think all my colleagues would agree that, by and large, the data show that there are well-defined, well-characterized benefits: from the reduction of pesticide use in some crops to increased yield and increased value to the growers. We've seen the very rapid adoption of the technologies by growers in those countries where they have been available. Certainly we have seen this in the U.S. with corn, soybean and cotton and with canola in Canada.

I think there are about double the acres of insect-resistant cotton planted in India as in the U.S., even though GM [genetically modified] cotton got a relatively late start there as compared with the U.S. I think in every country where growers have basically been able to "vote" in terms of what they would like, they have seen the benefits, and there has been this great adoption. That speaks volumes.

SA: But the standard rebuttal, as you know, is that the benefits of GM crops accrue lopsidedly to the seed producers and larger farms and not necessarily to the smaller farming interests, which may be more common in poorer regions.

SOYBEANS (*below, green*) planted with no-till technologies grow amid the stubble in a wheat field. Such no-till approaches can conserve precious topsoil.

BILL BARKSDALE *age fotostock (soybeans); MELISSA THOMAS (illustration)*

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"The big, big challenge in front of us in the next 40 years will be meeting the needs of the much larger population. You cannot meet that supply challenge without doing it sustainably."
—Antonio Galindez, Dow AgroSciences

What's disturbing to a lot of people is the economic side of the sustainability issue for these crops.

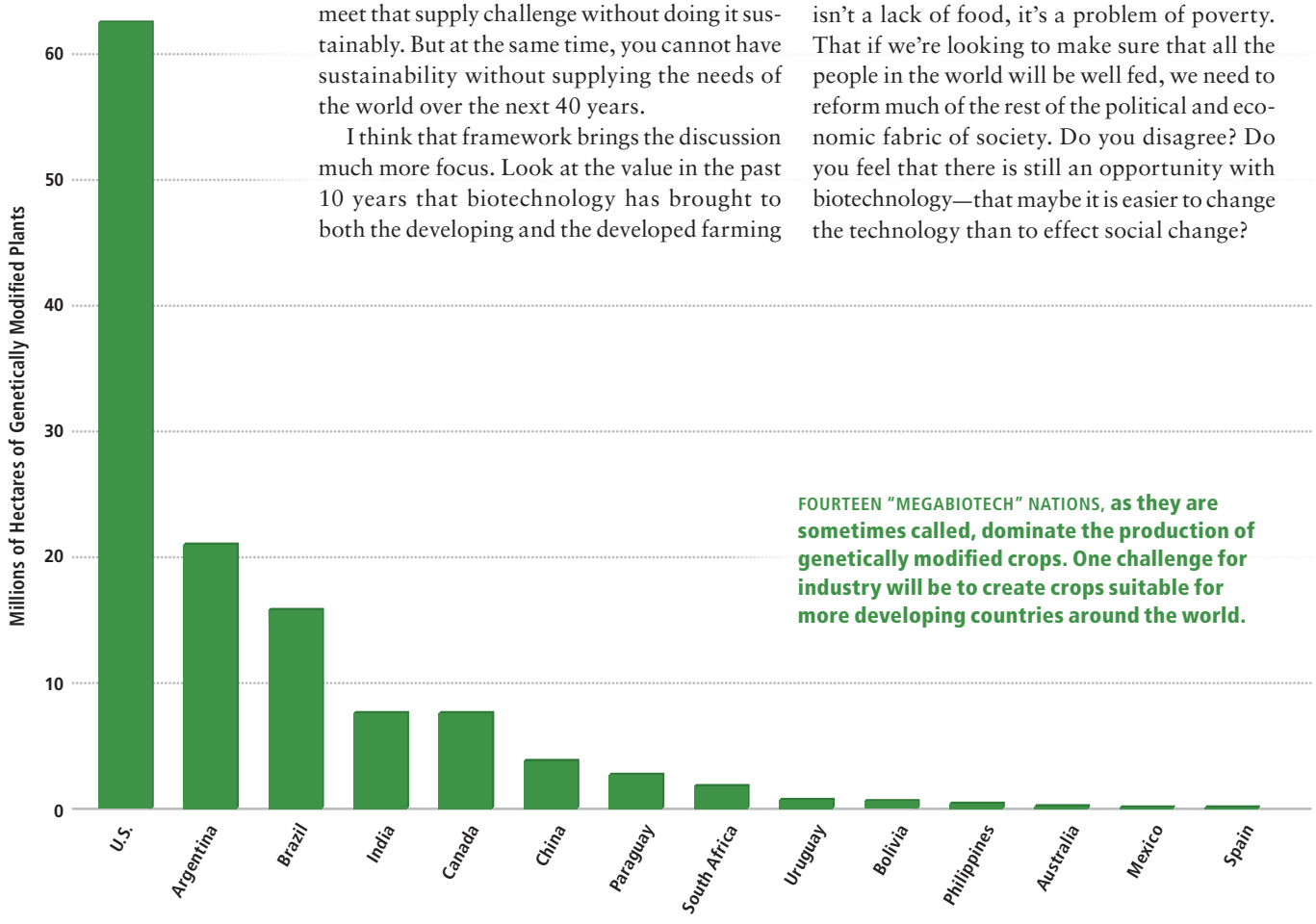
FISCHHOFF: There are, by our understanding, almost four million cotton growers in India who are raising insect-resistant cotton now, and they are growing cotton on a very, very small scale. We've seen similar adoption by small-scale growers in the Philippines. In South Africa we see it with insect-resistant cotton. Those are places where the value is clearly on the side of the grower, and I think our grower customers know that our products are priced to the value they deliver, whether the product involves a seed, or a genetically modified trait, or a new chemical or treatment. The growers get a very large share of that total value. Certainly we're all profit-making companies and we need to make money on what we produce, but I don't think it's disproportionately shared at all.

GALINDEZ: The big, big challenge in front of us in the next 40 years will be meeting the needs of the much larger population. You cannot meet that supply challenge without doing it sustainably. But at the same time, you cannot have sustainability without supplying the needs of the world over the next 40 years.

I think that framework brings the discussion much more focus. Look at the value in the past 10 years that biotechnology has brought to both the developing and the developed farming community. The biotech is not the only element; it's not the only tool in the box. But I think there are enough facts, if we want to look for them, that tell us that it has become one of the important tools. Together with machinery, together with irrigation technology, together with IT and the globalization of information, biotechnology is bringing the solution to both supply and sustainability.

FISCHER: It's not only about the benefits of the technologies that we develop but also the possible trade-offs that we would have to make. If we need to produce more food, we can do so either by bringing more acres into production, which is going to have an effect on the environment, or by increasing the efficiency and productivity of the current acres. I think the answer is clear: we should work harder to achieve greater productivity on the current acres using the best technologies available. But that is going to be a discussion we need to have as well.

SA: I'm sure you have all often heard the comment that the real cause of hunger in the world isn't a lack of food, it's a problem of poverty. That if we're looking to make sure that all the people in the world will be well fed, we need to reform much of the rest of the political and economic fabric of society. Do you disagree? Do you feel that there is still an opportunity with biotechnology—that maybe it is easier to change the technology than to effect social change?



FOURTEEN "MEGABIOTECH" NATIONS, **as they are sometimes called, dominate the production of genetically modified crops. One challenge for industry will be to create crops suitable for more developing countries around the world.**

MELISSA THOMAS; SOURCE: FRIENDS OF THE EARTH INTERNATIONAL, 2008; BASED ON DATA FROM FAOSTAT, 2007, AND ISAAA, 2008

CROPS MOST COMMONLY MODIFIED **include cotton, soybeans, corn and canola for its oil (*left to right*). The traits genetically engineered into them have mostly involved greater pesticide resistance.**

BOREL: Well, maybe if we start with Africa as an example, where there are a lot of people suffering from poverty and malnutrition, the technology can help. There are stories of farmers who have adopted hybrid technology in corn, and it's fundamentally changed their lives—their ability not just to feed their family but also to sell the crop and to have enough money to send their kids to school. There are amazing stories of impacts on people's lives with what, to us in the U.S., is fairly basic technology.

But it's more than just the technology. It takes access to credit. It takes land tenure. It takes insurance. It takes market access and communications. So certainly a focus we all have is to bring science to the market in a way that makes a difference. But I think—certainly at DuPont—we're also working with organizations to try to improve the infrastructure development and the local capability. In our case, we work directly with farmers in virtually all the countries in which we operate. In addition to the technology, it's working to help them get the right product on the right acre, whether in the center of Iowa or in a local area in Ethiopia.

FISCHHOFF: We can't solve all the world's poverty and food-distribution problems, but one of the things we can do is make sure that our technologies are accessible and available to farmers at all scales and in all countries.

One example is the way in which we can work with other organizations that are better able to address those problems. Monsanto has a partnership with some of the international agricultural institutes and with the Gates Foundation on delivering drought-tolerance technology in varieties and hybrids of corn adapted for Africa as quickly as possible after it is available to growers here in North America.

FISCHER: That's the same approach that we use in Syngenta. We develop our technologies and try to adapt them so that farmers all over the world can afford them. We have a policy of providing our technology, royalty-free, to benefit subsistence farmers in developing countries.

FISCHHOFF: We also can't ignore that we are now seemingly balanced just about equally between grain supply and grain demand every year. As the population increases, in order not to have more people be undernourished, we really need to keep this momentum for increasing yield and productivity going forward, or we'll be in an even worse situation.

BOREL: I think it surprises some people to realize that in 2008 more than 13 million farmers planted biotech crops. The surprise often comes when they realize that more than 12 million of those were small-scale farmers. There are still many countries where the traits and the advanced technologies aren't present yet, but there is a lot of work the industry is doing, and we as companies are doing, to get those technologies out where they can make a real difference regardless of the size of the farming operation. ■

STOCKBYTE/GETTY IMAGES (*cotton*); NEIL FLETCHER AND MATTHEW WARD *Getty Images* (*soya plant leaves*); BURAZIN *Getty Images* (*corn*); BODO A. SCHIEREN *Getty Images* (*oil bottle*)

Life is short...or maybe not.

Top Harvard researcher says it's "the Holy Grail of aging research."*

...as seen on CBS "60 Minutes"

Don't wait for the drug companies to drive the price through the roof; get the benefits of this breakthrough *natural* extract for pennies a day!

BOSTON, MA—Leading medical scientists are learning that resveratrol, a natural substance found in red wine, is rewriting the rules on the science of aging.

Researchers at the **Harvard Medical School** and the **National Institute on Aging** already discovered that the red wine extract offset the negative effects of a high-calorie diet in mice and significantly extends their life span (*NY Times*, Nov 2, 2006). Now, the latest research indicates that resveratrol may been even more powerful than first anticipated.

At this moment, drug companies are rushing to create prescription drugs that mimic the awesome health benefits of this simple natural extract. A leading pharmaceutical company has already spent $760,000,000 on purchasing the research and development.

The powerful secret of tomorrow's anti-aging pill can be yours today.

You may have thought that an anti-aging pill would only be available far into the future. But the effects of resveratrol have been proven as scientific fact... today. Even better, resveratrol is a naturally-occurring substance found in the skin of grapes and red wine, not manufactured in some laboratory. The key to living longer may be found inside your favorite bottle of red wine.

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"We have something (resveratrol) that **extends the life of every species** it's (been) given to. We're 50 years ahead of where I'd thought we would be 10 years ago," said a leading professor of pathology at Harvard Medical School, reported by the *NY Times*.

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Has the "The French Paradox" finally been explained?

Resveratrol is conjectured to be a partial explanation for "The French Paradox," the puzzling fact that people in France enjoy a high-fat diet yet suffer less heart disease than Americans and live significantly longer lives (in some cases up to 40%).

Even though French diets are crammed with loads of bread, cheese, rich cream sauces and decadent desserts... the resveratrol in red wine may have acted as their secret weapon. It is thought that the resveratrol protected them against unhealthy triglycerides, high cholesterol and skyrocketing blood pressure.

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Harvard Medical School, Johns Hopkins, Salk Institute and UC Davis Medical Research Proves That Powerful Red Wine Extract Holds the Secret to Living a Longer, Healthier and More Vibrant Life

*These statements have not been evaluated by the FDA. This product is not meant to diagnose or treat any disease. Vinotrol is not endorsed, associated or affiliated in any way with Harvard University, Johns Hopkins, Salk Institute or UC Davis Medical. * CBS News, Nov 1, 2006*

*Why do **whales beach** themselves? Are strandings increasing?*

Darlene Ketten, a neuroethologist at the Woods Hole Oceanographic Institution, lays out an explanation:

I often use the analogy of a car crash: a lot of things can cause a crash, but you get the same end result. We can determine the cause of a stranding in only about 50 percent of all cases. In those, sometimes the cause is obvious, such as when a ship strike leaves an animal with distinctive fractures and gashes. In the northeastern U.S., pneumonia and trauma after storms are common reasons. We see other trauma as well, including shark attack or even assaults by members of the same species. Both human-derived pollutants and natural toxins, such as neurotoxins from algae, are implicated in mass strandings. Anomalies in magnetic fields and tsunamis have also been suggested as causes.

Some of the most fascinating cases stem from diseases and congenital conditions. We see parasites and pathologies far more severe than in domestic animals or humans. It is surprising that individuals can last as long as they do with such conditions.

Military sonars have clearly contributed to some recent strandings of beaked whales, but no evidence supports assertions that all whales are being affected by sonar. Interestingly, only beaked whales appear to be affected and only in a few locations—which offers hope of solving that problem at least.

Then there are cases with no single, clear answer. Diagnostic techniques common in human medicine, such as CT and MRI scanning and molecular studies, are now being used to improve insight into the causes.

We know of whale strandings dating back to the time of Aristotle, which implies that most are a natural phenomenon. That raises a question: If you insist on returning an animal to the sea, are you harming the population? If the animal is sick, what are we doing to that population pool? I'm not advocating failing to rehabilitate animals, if we can, but the issue is an important one to consider.

BEACHED WHALES in Cape Town, South Africa

NIC BOTHMA *EPA/Corbis*

What to Do?

On the other hand, if a human activity precipitates a stranding, we need to know about it—to make decisions about pollutants, shipping routes and noise. Are we in some way contributing to declining health of critical populations, such as the northern right whale with fewer than 400 individuals left? We certainly have more reports of strandings, and people are looking into whether there are more instances or just more reports in some areas.

Sometimes, regardless of the cause, the only real option is to euthanize the animals—as was done in May after false killer whales that had washed onto land near Cape Town, South Africa, defied efforts to get them back out to sea. Imagine struggling to get those animals back in water in winter conditions. Though large, they are in some ways very fragile. For instance, if you get sand or water down their blowhole when handling them, the effect is like having water squirted up your nose. If you get the animal back into the water and it swims off but weakens and returns two or three times to shore, the decision will have to be made whether it can survive or is suffering, and a veterinarian must end its life humanely. ■

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

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BY KATE WONG

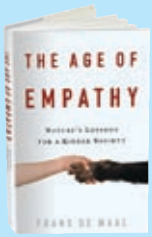
THE SIBLEY GUIDE TO TREES
by David Allen Sibley. Knopf, 2009 ($39.95)

Naturalist and illustrator David Allen Sibley, best known for his guides to birds, turns his attention to the bark, leaves, fruits and flowers of more than 600 species of North American trees, such as the shagbark hickory (*detail*).

FROM *THE SIBLEY GUIDE TO TREES*, COURTESY OF ALFRED A. KNOPF

EXCERPT

THE AGE OF EMPATHY: NATURE'S LESSONS FOR A KINDER SOCIETY
by Frans de Waal. Harmony Books, 2009 ($25.99)



Grieving elephants, sympathetic bonobos, grateful whales—nature is not always red in tooth and claw. In his latest book primatologist Frans de Waal draws on numerous examples from our fellow fauna, such as the chimpanzee in the anecdote below, to make his case that humans are hard-wired to be humane.

"… don't believe anyone who says that since nature is based on a struggle for life, we need to live like this as well. Many animals survive not by eliminating each other or by keeping everything for themselves, but by cooperating and sharing. This applies most definitely to pack hunters, such as wolves or killer whales, but also our closest relatives, the primates. In a study in Taï National Park, in Ivory Coast, chimpanzees took care of group mates wounded by leopards, licking their blood, carefully removing dirt, and waving away flies that came near the wounds. They protected injured companions, and slowed down during travel in order to accommodate them. All of this makes perfect sense given that chimpanzees live in groups for a reason, the same way wolves and humans are group animals for a reason. If man is wolf to man, he is so in every sense, not just the negative one. We would not be where we are today had our ancestors been socially aloof.

"What we need is a complete overhaul of assumptions about human nature. Too many economists and politicians model human society on the perpetual struggle they believe exists in nature, but which is a mere projection. Like magicians, they first throw their ideological prejudices into the hat of nature, then pull them out by their very ears to show how much nature agrees with them. It's a trick for which we have fallen for too long. Obviously, competition is part of the picture, but humans can't live by competition alone."

ALSO NOTABLE

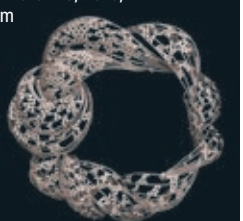
BOOKS

- **The Age of Wonder: How the Romantic Generation Discovered the Beauty and Terror of Science**
  by Richard Holmes. Pantheon, 2009 ($40)
- **The Greatest Show on Earth: The Evidence for Evolution**
  by Richard Dawkins. Free Press, 2009 ($30)
- **Uranium Wars: The Scientific Rivalry That Created the Nuclear Age**
  by Amir D. Aczel. Macmillan, 2009 ($27)
- **Rising Plague: The Global Threat from Deadly Bacteria and Our Dwindling Arsenal to Fight Them**
  by Brad Spellberg. Prometheus Books, 2009 ($26)
- **Something Incredibly Wonderful Happens: Frank Oppenheimer and the World He Made Up**
  by K. C. Cole. Houghton Mifflin Harcourt, 2009 ($27)
- **Total Recall: How the E-Memory Revolution Will Change Everything**
  by Gordon Bell and Jim Gemmell. Dutton, 2009 ($26.95)
- **Hope for Animals and Their World: How Endangered Species Are Being Rescued from the Brink**
  by Jane Goodall, with Thane Maynard and Gail Hudson. Grand Central Publishing, 2009 ($27.99)

- **Connected: The Surprising Power of Our Social Networks and How They Shape Our Lives**
  by Nicholas A. Christakis and James H. Fowler. Little, Brown, 2009 ($25.99)

EXHIBITS

- **The Nature of Diamonds**
  October 23, 2009–March 28, 2010, at the Field Museum in Chicago.



COURTESY OF PHILIP HERSEE PHOTOGRAPHY

- **Darwin Center**
  This permanent science and collections facility opens September 15, 2009, at the Natural History Museum in London.

Birth of a Notion

Deeply held beliefs make it easy to accept the absurd

BY STEVE MIRSKY

Once, while visiting Brooklyn, I got a call from a fellow Bronxite, back on the mainland. When I revealed my location, he said, "Brooklyn?! What time is it there?" Despite the interborough bafflement, Brooklyn has been a genuine part of the land of the free since day one, that is, July 4, 1776. So when Lena Horne was born there in 1917, she automatically became a U.S. citizen. About 25 years later Horne was asked to give two concerts at Camp Robinson in Alabama, one to white servicemen, the second to black GIs. But she refused to do the second one when she saw that black Americans were sent to the back of the theater. Who got the good seats up front? German prisoners of war. Journalist Nat Brandt's book *Harlem at War: The Black Experience during World War II* quotes Horne as summing up the situation thusly: "Screw this."

Today, of course, the commander in chief of the U.S. military is black, and President Barack Obama gets the best seats in the house. A black president, however, causes great cognitive dissonance in some. But members of the "birther" movement have found a clever solution: Obama isn't really president! Because he wasn't really born in the USA!

Of course, he was, in Hawaii. (What time is it *there*?) So how could millions of people—a recent Daily Kos/Research 2000 poll found that 58 percent of Republicans, mostly concentrated in the South, either don't believe or aren't sure Obama is a citizen—be persuaded that the president is foreign? And how could high-ranking officers treat white enemies better than black patriots?

A part of the answer may lie in what's called implicit social cognition, which involves the deep-rooted assumptions we all carry around and even act on without realizing it. Harvard University psychologist Mahzarin Banaji is a leader in implicit social cognition research. She excavates the hidden beliefs people hold by measuring how fast they make value judgments when shown a rapid-fire succession of stimuli, such as photographs of faces.

At a talk she gave in October 2008 to a group of science journalists, Banaji discussed research she did with Thierry Devos, now at San Diego State University, that examined bias against Asians. They found that volunteers linked white Americans more strongly than Asian-Americans with, well, America. Banaji and Devos then decided to do what even they thought was a "bizarre" study: they had people gauge the "American-ness" of famous Asian-Americans, such as Connie Chung and tennis player Michael Chang, versus European whites, such as Hugh Grant.

The study found that white Europeans are more "American" than are nonwhite Americans in most minds. (Which brings to my mind former vice president Dan Quayle, who mangled the United Negro College Fund slogan into "What a waste it is to lose one's mind, or not to have a mind is being very wasteful.")

That result helps to explain how MSNBC's Web site in 1998 could have run the remarkable headline "American Beats Out Kwan" with a story on how Tara Lipinski defeated fellow American Michelle Kwan in a figure skating competition. A *Seattle Times* article quoted the then director of the Japanese American Citizens League, reaching for a silver lining: "Maybe there's a little progress in that they don't see Lipinski as a foreign name anymore."

Little surprise, then, that in a study done during the 2008 election campaign, Devos found that John McCain (who, ironically, was born in Panama, albeit at a U.S. naval base) was seen as more "American" than Obama. But even British ex–prime minister Tony Blair was seen as more "American" than Obama, a finding that nearly made me spit out me bangers 'n' mash.

To borrow terminology from Obama's health care proposals, the birthers thus appear to suffer from a preexisting condition. A possible treatment is a recording by Aretha Franklin, who had no reason not to perform at Obama's inauguration. The song is entitled "Think." Because a mind is a terrible thing to waste. ■

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30 WORDS THAT CHANGED THE WORLD

"I believe this nation should commit itself to achieving the goal before this decade is out of landing a man on the Moon and returning him safely to the Earth."

WHEN President Kennedy spoke those 30 simple words during a speech to a Joint Session of Congress on May 25, 1961, he launched an era of exploration and an achievement that has yet to be equaled. The mission was clear: put a man on the Moon. But how? That was the big question.

We all know the ending of that story: July 20, 1969. Those who were there to see those grainy black-and-white images of Neil Armstrong taking his first small step remember it vividly. Those who weren't, can only imagine the excitement. We had done it.

Today, there is a new mission facing us. A new quest that is as important – and as difficult – as our journey to the Moon. The goal: energy security. What is it going to take to reach this destination?

Energy efficiency. Alternative fuels. Renewable energy. Grid management. Energy storage. Conservation. Climate monitoring. There is no single path toward energy security. There are many. And we must explore all of them in order to meet the nation's goal of 15% renewable energy by 2020 and 80% reduced greenhouse gas emissions by 2050.

It won't be easy. But then, as JFK said, "We choose to go to the Moon in this decade and do the other things, not because they are easy, but because they are hard."

Solving our nation's energy and climate challenges will require the same level of commitment as the space race, which brought us together as a nation and inspired generations of students to take up the study of science, math, and engineering.

As part of the team that helped NASA achieve the Apollo 11 landing, Lockheed Martin has a history of supporting national priorities. We know about mobilizing resources to attack highly complex problems. Our scientists and engineers have tackled many daunting tasks. Including helping to put a man on the Moon. In fact, the communication system that broadcast Armstrong's famous first words was built by a Lockheed Martin legacy company. Closer to home, our satellites have kept an eye on the environment for the past half-century and our team has been helping manage energy labs for close to three decades.

Today, men and women across our corporation continue to put their minds to the very urgent matters of energy security and climate change. They are helping regulated utilities and federal agencies implement energy efficiency programs. Researching ways to generate clean energy using everything from ocean temperatures to concentrated solar power. Even exploring how to capture solar power from space, where the sun always shines. We're leveraging our experience in command and control and cyber security to help customers manage and distribute power more smartly and securely here on the ground. And building partnerships in industry and academia to create original solutions. Because that's what we do best.

In the end, what does energy security really mean? At Lockheed Martin, we believe it means more than "going green." Or avoiding blackouts. We believe that energy security will support a strong economic future and climate protection for future generations. We believe that breaking our dependence on foreign oil will be the pillar of our nation's security and a key component of global security.

That is why, as a global security company, we believe that we have the ability and responsibility to apply the broad spectrum of our capabilities to the "space race" of this generation.

You often hear people use the phrase "if we can put a man on the Moon …" to express America's can-do spirit. Well, we did help America put a man on the Moon. When America asked "How?" we answered. And we are here now, 40 years later, helping take the small steps and giant leaps that will secure our nation's energy future.

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