SCIENTIFIC AMERICAN

April 2011 ScientificAmerican.com

Antibiotics
New Threat from Lethal Bacteria

Imaging
Neuroscience in the Courts

Seismology
Earthquake Warning System

Quantum Gaps in Big Bang Theory

Why our best explanation of how the universe evolved must be fixed—or replaced

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SCIENTIFIC AMERICAN

April 2011 Volume 304, Number 4

ON THE COVER

The well-tested theory of cosmic inflation holds that the universe has the structure we know and love because the early universe underwent a period of incredibly rapid expansion. Now a leading contributor to the concept confesses that he and other scientists have been sweeping important problems with the theory under the rug. Illustration by Malcolm Godwin.

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KENNETH C. CATANIA

The Most. Fuel-Efficient. Midsize. Sedan. In. America.

What does that mean exactly?

It means the 41 city mpg 2011 Fusion Hybrid has a lot to say.

Seriously,
just look at that claim, will you?
It's quite the loaded statement.

Let's break it down.

First off,
don't overlook the fact that it's a *2011*. It's easy to do, but *2011* means it's new. Shiny and fresh, full of promise and possibilities.

Next
– and this is a big one –
it's the *most* fuel-efficient.
That means it has best-in-its-class mpg.
And how many can say they're the best in their category? Usually only one. And in this case, it's the Fusion Hybrid.

And Fusion is the most fuel-efficient ***in America***, which is a pretty big place, with a lot of potential competition. Or not much competition at all, depending on how you're measuring it.

Either way, it's definitely good news for Ford, for Fusion and for its drivers.

Think about it –
who wouldn't love the Fusion Hybrid getting 41 city mpg?
Well, now that we think about it, the 2011 Camry Hybrid, for one.
Fusion beats it by a full 10 mpg in the city.

OK, so sure, Camry probably isn't one of Fusion's biggest fans. But, since Fusion is a hybrid, let's hope we can find common ground in the fact that

its superior fuel economy
(sometimes it uses no gas at all!)
is better for the environment.

So, in the grand scheme of things, the 2011 Fusion Hybrid is doing some good for all of us. Even for the 2011 Camry Hybrid. You're welcome, Camry Hybrid.

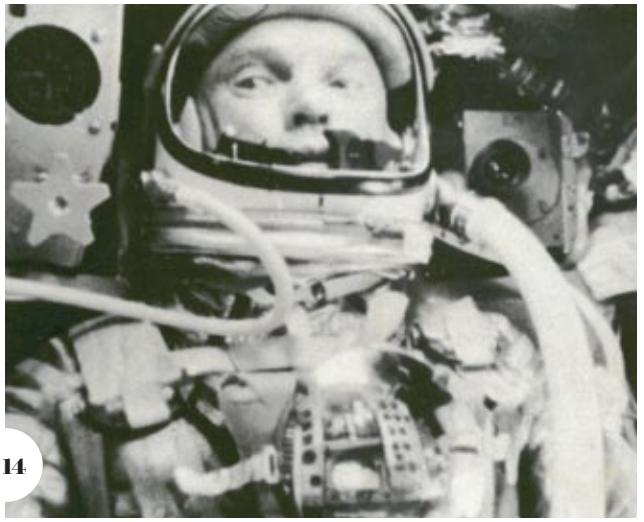
So there you have it.
THE 2011 FUSION HYBRID
The most fuel-efficient midsize sedan in America.*

If you're thirsty for more fuel economy info, you can find more of it, plus reactions from real Fusion owners, at
ford.com.

*EPA-estimated 41 city/36 hwy/39 combined mpg. Actual mileage will vary. Midsize class per R. L. Polk & Co. vs. 2010/2011 competitors.

Ford

Drive one.



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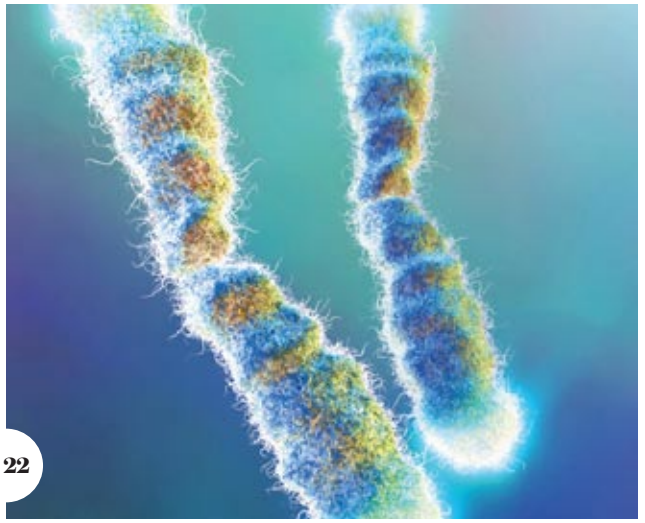

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ON THE WEB

Rolling the Dice on Energy Technology
Federal and private funders met with energy innovators at the second summit of the Advanced Research Projects Agency–Energy, a U.S. government body dedicated to research with long odds—and big potential payoffs.
Go to www.ScientificAmerican.com/apr2011/arpae

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Mariette DiChristina is editor in chief of *Scientific American*. Find her on Twitter @SAeditorinchief

Reflections from Science

Science, it is sometimes claimed, is neutral: it is up to society to decide how to employ research findings. Yet society often struggles with its end of the deal. That is because science can also hold up a mirror to the results of our culture's choices—and we may not like what we see.

Consider antibiotics. Since their discovery decades ago, these "wonder drugs" have been used far more widely than for the treatment of sick patients. Tourists take them when they go on vacation to prevent traveler's diarrhea. We give them to livestock, helping to keep our meats cheap.

The microbes that have survived this selection pressure are now demonstrating a disturbing new pattern of resistance—and sometimes complete immunity even to last-resort medicines. Bacteria share genes freely, widening the global threat. Meanwhile pharmaceutical companies do not have drugs in the pipeline to combat the new bug strains. Hospitals have had to increase infection controls. Are we entering a postantibiotic world? Turn to page 46 for Maryn McKenna's sobering article, "The Enemy Within."

In Science Agenda, on page 12, the board of editors suggests a way to reduce the development of further resistance: stop dosing pigs, chickens and other farm animals with subtherapeutic amounts of antibiotics. The U.S. can take a lesson from Denmark, which has efficiently raised livestock without hurting farmers, by using better animal husbandry practices.

Last, brain scans have transformed our understanding of cognitive processes. Could they factor into trials, by providing insights into an accused's mental state? Michael S. Gazzaniga considers the challenges involved in "Neuroscience in the Courtroom," on page 54. As it turns out, neuroscience's greatest influence may be in identifying root causes of illegal behaviors. But the choice of how to use the science is, ultimately, also society's to make. SA

UPDATE

BRING SCIENCE HOME

A few months ago I wrote about *Scientific American*'s participation, as a part of Nature Publishing Group, in Change the Equation. This CEO-led initiative, part of the White House's Educate to Innovate program, seeks to boost learning in science, technology, engineering and mathematics (STEM). Soon we will be launching our first related project, called Bring Science Home.

A challenge of improving our nation's performance in science education is that children who get turned off at a young age may never come back. And studies have found that even in kindergarten, students are forming negative views about science [see "Start Science Sooner," SA Perspectives; Scientific American, March 2010]. I thought: How can non-STEM parents help foster STEM-loving kids?

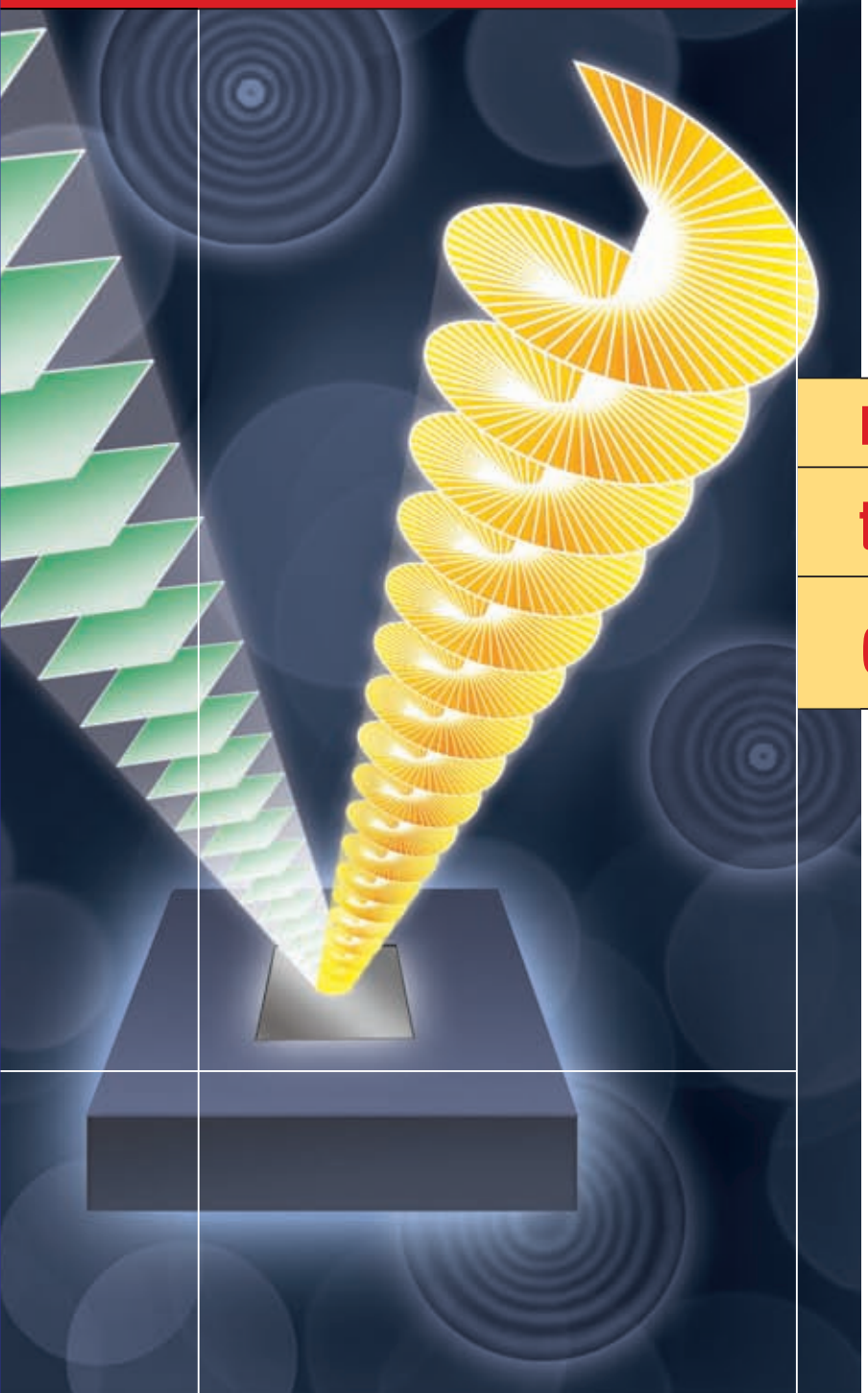
That was the inspiration behind Bring Science Home, led by Katherine Harmon of our online team. For the month of May, www.ScientificAmerican.com will feature one science-related activity each weekday, which parents and their six- to 12-year-olds can do together. We consulted with members of the National Science Teachers Association so that the activities would echo themes taught in early grades. Parents will also find additional background to help them explain the concepts. But the overarching goal was simple: each activity had to be easy and fun, done with household ingredients and completed in less than an hour.

In the next issue, I will update you on other STEM efforts.

—M.D.

Illustration by Nick Higgins

Now there's an easier way to put a precise spin on "twisted light"



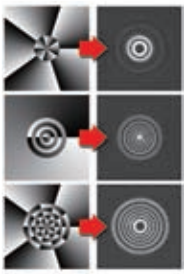
Advancing twisted light applications

Usually we think of light as traveling in a straight path, in a train of parallel planes called *wavefronts*.

But light can also be twisted into helix-shaped wavefronts for many useful new applications.

The challenge is how to *precisely control* the twisting of the light—*and* do that with equipment that is flexible and widely usable.

Hamamatsu created an elegantly simple solution...



Special phase profiles (left) twist light into the beam patterns at right.

Their *Liquid Crystal on Silicon Spatial Light Modulator* (LCOS-SLM) uses a computer to precisely shape the reflective profile of a liquid crystal surface. Applying special phase profiles to that surface will twist the reflected light in precisely controllable ways. Yet the system is compact, cost-efficient and easy to use.

Hamamatsu is opening the new frontiers of Light

Hamamatsu's LCOS Spatial Light Modulator

Which may help scientists in developing new twisted light applications...

Such as new computers that employ the infinite quantum states of optical vortices to process data. Or new generations of quantum communications and data encryption. Or "optical tweezers" that can manipulate cells and other micro particles...

Twisted light: It's another exciting new frontier that Hamamatsu is helping to open!

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

HAMAMATSU

PHOTON IS OUR BUSINESS

Hamamatsu's computer-controlled Liquid Crystal on Silicon Spatial Light Modulator (LCOS-SLM) is able to very precisely convert a straight beam of light into a twisted, helix-shaped beam for use in many advanced applications.

editors@sciam.com

December 2010

DISAGREEING ON EVERYTHING

As theoretical physicists, we deplore the publication of A. Garrett Lisi and James Owen Weatherall's "A Geometric Theory of Everything," as well as of Zeeya Merali's "Rummaging for a Final Theory" [News Scan] in the September issue, which was PR-level praise of Lisi's research that presented him as struggling against an entrenched establishment.

As you surely knew Lisi's views to be, to say the least, controversial, basic editorial precaution would have required first consulting a reputable particle physicist. You would have learned that duly refereed and published work of Jacques Distler of the University of Texas at Austin and Skip Garibaldi of Emory University has shown that Lisi's model cannot even reproduce parity violation.

This effect, experimentally verified more than 50 years ago, is a basic element of the overwhelmingly successful Standard Model of particle physics. Instead Lisi predicts a host of particles that have not been detected and fails to account for the existence of other particles that do exist. His model simply fails to provide any correct physics.

Stanley Deser, Albion Lawrence and Howard J. Schnitzer
Brandeis University

THE EDITORS REPLY: Merali's article covered a scientific meeting on new algebraic approaches to unifying physics, one of which is Lisi's. She acknowledged his theory to be controversial, mentioning the work by Distler and Garibaldi, even quoting Garibaldi himself. She also quoted Lisi's response, in which he said his ideas are still works in progress and sketched a possible solution to the criticism.

Separately, we had invited Lisi and Weatherall to describe Lisi's work for the benefit of readers who may have been curious about it after seeing its geometric beauty hinted at elsewhere. We did so in the spirit of presenting fresh ideas that are illuminating if admittedly tentative—one notable example being Scientific American*'s articles on string theory in its early days. That decision was made after consultation with experts, most of whom were indeed skeptical about Lisi's theory, but some of whom still thought it promising.*

"Allowing patients to alter their entire life outlook based on experiences with hallucinogens is, I think, fundamentally unethical."
BEN HALLER *McGILL UNIVERSITY*

SKEPTICAL ABOUT FLUORIDE

I was saddened to see the inclusion of water fluoridation in Michael Shermer's "The Conspiracy Theory Detector." Perhaps Shermer should go back and look at *Scientific American*'s own coverage of fluoride [see "Second Thoughts about Fluoride," by Dan Fagin; January 2008] or, better still, read the science in the 2006 National Research Council report "Fluoride in Drinking Water: A Scientific Review of EPA's Standards."

I have seen and read the science, and I no longer drink and cook with my city's fluoridated water supply. I wish I could afford to not be forced to wash in it. Incidentally, carbon filters such as Brita's do not remove fluoride from the water, and boiling it makes the fluoride more concentrated. Infants exposed to fluoride could have reduced IQ. Can our society really afford to take that chance?

Greg Warchol
Oakville, Ontario

GOOD AND BAD TRIPS

In "Hallucinogens as Medicine," Roland R. Griffiths and Charles S. Grob describe the therapeutic benefits of hallucinogens such as psilocybin and LSD, as well as some of their risks. I was surprised, however, to see no discussion of perhaps the largest risk: causing patients to form false beliefs. Patients in the studies they cite emerge from their hallucinogenic experience believing that "all is One," that "God asks nothing of us except to receive love," and having a "peculiar disregard for … their impending death."

Indeed, having used both psilocybin and LSD myself, I have experienced these states. Not only did I have a disregard for my own death, I spent half an hour during one trip considering whether I ought to chew off and eat my own fingers. Happily, I chose not to, and overall I recall the trips of my youth fondly. But the visions they gave me were not real or true; they were the result of overstimulation of specific brain centers by a chemical. Allowing credulous patients to alter their entire life outlook and philosophy based on such experiences is, I think, fundamentally unethical, whatever the positive side effects might be.

Imagine if a study proposed to hypnotize patients, to tell them to believe all sorts of nonsense, and then to wake them up and leave them with those beliefs for the rest of their lives because it was expected that the nonsense beliefs would produce positive clinical outcomes. Would such a proposal pass an ethical review panel? I would certainly hope not. That situation is precisely parallel to the hallucinogen studies, except that instead of the doctor whispering falsehoods into the patient's ear, it is the drug given by the doctor.

Ben Haller
Department of Biology
McGill University

GRIFFITHS AND GROB REPLY: We were glad to read that Haller did not eat his fingers. This is not surprising, however, as hallucinogen-involved trauma is very rare under the haphazard conditions of illicit use—which we nonetheless caution against—and it is virtually unheard of

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Chris
CITGO Owner
Climax, NC

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within supervised research settings. Haller dismisses the philosophical statements by psilocybin study volunteers as "false." We regard them as unfalsifiable, and so, as scientists, we take no position for or against them. We do note, without judgment, that they tend to align with the mystical teachings of the world's religions. The analogy with hypnosis is spurious, because in our psilocybin sessions we do not introduce explicit content to the patient.

During informed consent, candidate volunteers learn up front of psilocybin's potential effects, including lasting changes in philosophy and outlook. Our ethics committees have approved our studies, which we stand behind. The risk-to-benefit assessment for this research is favorable. Preliminary studies in patients and healthy volunteers suggest substantial and sustained positive effects.

THE ROAD MORE TRAVELED

In "Know-It-All Toll Roads" ["World Changing Ideas"], Tom Vanderbilt claims pricing the roads is a better alternative to sitting in traffic. We thoroughly disagree. Free-market principles work fine for commodities that can be produced by several competitors, such as TVs. For public goods such as roads, however, there is usually only one best route and all others are much less desirable. "Ration by queue" gives all people equal access to the best option. The fact that so many people are willing to sit in traffic is proof those routes are more desirable for everyone. With "ration by price," only the rich could afford the desirable routes. It sounds like an absolutely terrible idea and would set a dangerous precedent.

Steven and Luci Jones
Rocklin, Calif.

ERRATUM

In Michael Shermer's "The Conspiracy Theory Detector" [Skeptic], a quote by Anthony J. Hall uses the word "economy" but should have said "academy." Also, the "[sic]" annotation should be disregarded.

CLARIFICATION

In the February issue we printed a letter by Devra Davis mentioning the University of Pittsburgh as her affiliation. That was correct when the issue went to press but not by the time it came out. Davis is at the Environmental Health Trust.

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Our Big Pig Problem

The U.S. should follow Denmark and stop giving farm animals low-dose antibiotics

For more than 50 years microbiologists have warned against using antibiotics to fatten up farm animals. The practice, they argue, threatens human health by turning farms into breeding grounds of drug-resistant bacteria. Farmers responded that restricting antibiotics in livestock would devastate the industry and significantly raise costs to consumers. We now have empirical data that should resolve this debate. Since 1995 Denmark has enforced progressively tighter rules on the use of antibiotics in the raising of pigs, poultry and other livestock. In the process, it has shown that it is possible to protect human health without hurting farmers.

Farmers in many countries use antibiotics in two key ways: (1) at full strength to treat animals that are sick and (2) in low doses to fatten meat-producing livestock or to prevent veterinary illnesses. (It is illegal in the U.S. to sell milk for human consumption from dairy cattle treated with antibiotics.) Although even the proper use of antibiotics can inadvertently lead to the spread of drug-resistant bacteria, the habit of using a low or subtherapeutic dose is a formula for disaster: the treatment provides just enough antibiotic to kill some but not all bacteria. The germs that survive are typically those that happen to bear genetic mutations for resisting the antibiotic. They then reproduce and exchange genes with other microbial resisters. Because bacteria are found literally everywhere, resistant strains produced in animals eventually find their way into people as well. You could not design a better system for guaranteeing the spread of antibiotic resistance.

The data from multiple studies over the years support the conclusion that low doses of antibiotics in animals increase the number of drug-resistant microbes in both animals and people. As Joshua M. Sharfstein, a principal deputy commissioner at the Food and Drug Administration, told a U.S. congressional subcommittee last summer, "You actually can trace the specific bacteria around and … find that the resistant strains in humans match the resistant strains in the animals." And this science is what led Denmark to stop subtherapeutic dosing of chickens, pigs and other farm animals.

Although the transition unfolded smoothly in the poultry industry, the average weight of pigs fell in the first year. But after Danish farmers started leaving sows and piglets together a few weeks longer to bolster the littermates' immune systems naturally, the animals' weights jumped back up, and the number of pigs per litter increased as well. The lesson is that improving animal husbandry—making sure that pens, stalls and cages are properly cleaned and giving animals more room or time to mature—offsets the initial negative impact of limiting antibiotic use. Today Danish industry reports that productivity is higher than before. Meanwhile reports of antibiotic resistance in Danish people are mixed, which shows—as if we needed reminding—that there are no quick fixes.

Lest anyone argue that Denmark is too small to offer a reasonable parallel to the U.S., consider that it is the world's largest exporter of pork. Like U.S. farmers, Danes raise pigs on an intensive, industrial scale. If they can figure out how to limit antibiotic use while actually increasing agricultural productivity, then so can Americans.

The American Medical Association, the Infectious Diseases Society of America, the American Public Health Association, a previous FDA commissioner and many others have advised the U.S. to follow suit. Last year the FDA published new guidelines calling for "judicious use" of antibiotics. Yet it ultimately left the decision on exactly when and where to use antibiotics up to individual farmers. That laissez-faire standard is not good enough, particularly when the health of the rest of the population is at stake.

Of course, the way veterinary antibiotics are used is not the only cause of human drug-resistant infections. Careless use of the drugs in people also contributes to the problem. But agricultural use is still a major contributing factor. Every day that passes brings new evidence that we are in danger of losing effective antibiotic protection against many of the most dangerous bacteria that cause human illness [see "The Enemy Within," by Maryn McKenna, on page 46]. The technical issues are solvable. Denmark's example proves that it is possible to cut antibiotic use on farms without triggering financial disaster. In fact, it might provide a competitive advantage. Stronger measures to deprive drug-resistant bacteria of their agricultural breeding grounds simply make scientific, economic and common sense. SA

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Lawrence M. Krauss is Foundation Professor and director of the Origins Project at Arizona State University and an author, most recently of *Quantum Man*.

Rethinking the Dream

Fifty years after the first human ventured into space, we need some creative thinking

I still remember the excitement and fear of April 12, 1961, the day Yuri Gagarin became the first human to travel into space. I was seven years old: too young to fully appreciate the thrill many people felt that the mysterious universe beyond Earth had suddenly been conquered and that the adventures of the swashbuckling Flash Gordon were now one step closer to reality. I was old enough, however, to vividly remember concern that the first person in space was Russian and not American.

The decade that followed Gagarin's pioneering foray above the atmosphere seemed to validate all the promises of space travel I had gleaned from science fiction. Before the end of the decade men would walk on the moon, and the future, depicted most explicitly—and, we all thought, realistically—in *2001: A Space Odyssey,* seemed so bright we needed shades. During each of the Apollo flights, I stayed home from school, huddled in the basement near the television with the diagrams of rockets I had cut out of local newspapers and magazines, transfixed by the images from space. I imagined the possibility that one day I, too, might experience the excitement of space travel.

John Glenn orbited Earth the year after Yuri Gagarin's flight.

Alas, it was not to be. Human space exploration has been reduced to visiting a $100-billion tin can orbiting closer to Earth than Washington is to Boston. No one except a billionaire or two has ever vacationed in space, and their "hotel" was a cramped, stuffy and at times smelly white elephant. The moon is not being mined for rare or expensive elements. Aside from communications satellites, space is devoid of industry.

What happened? Why did the dream of unlimited manned space travel and a vast new universe of possibilities for humanity dry up and fizzle? The answer is relatively simple: reality prevailed. Human space travel is expensive and dangerous, and there is almost no scientific justification for it (a sobering realization for the child-turned-scientist). All these factors stem from the same problem: most of the incredible cost of human space travel goes into keeping humans alive during the process, leaving little money for other things. This harsh reality leaves those of my generation in a position, 50 years hence, of having to reevaluate those childhood dreams.

It is important to acknowledge, first of all, that advances have been made. We have sent robots to places humans could never have survived and peered into the cosmos with instruments far more capable than our human senses, all for a small fraction of what it costs to send a living, breathing person into Earth's orbit. The first rovers went to Mars for what it would cost to make a movie about sending Bruce Willis to Mars. And the Hubble Space Telescope, perhaps the most important and expensive unmanned device sent into space thus far, has captured our imagination in a way the International Space Station never has. And our robotic technology continues to improve.

This is not to say that sending humans into space is entirely pointless. If our species is to survive, our future will probably require outposts beyond our own planet. And having shared the stage with many an astronaut, I can attest to how inspiring they can be. Their exploits were precisely what got me so excited when I was a kid and helped to spur me to become a scientist.

Sending people into space for the sake of adventure and perhaps eventual habitation is a legitimate goal. But if we are to undertake it, we should be honest about our reasoning. Pretending that space voyages will push forward the frontiers of science or provide vast new opportunities to tap cheap or scarce resources is disingenuous. If inspiration is what we are after, let us do inspiring things—not orbit endlessly around Earth.

Figuring out how to inspire, in this age of preoccupation with debt and unemployment, is not going to be easy. We need new ideas. Establishing a permanent presence on Mars, to take one example, will cost many tens of billions of dollars. Such a mission is at present inconceivable, unless we can rethink it.

I have suggested, for example, sending astronauts on a one-way mission. Even if we consider the cost of keeping the crew alive indefinitely on the planet's surface, a one-way trip would cost a mere fraction of a two-way trip, and I am sure volunteers would line up. If we are going to break the cycle of disappointment, we are going to need all the creative thinking we can muster. SA

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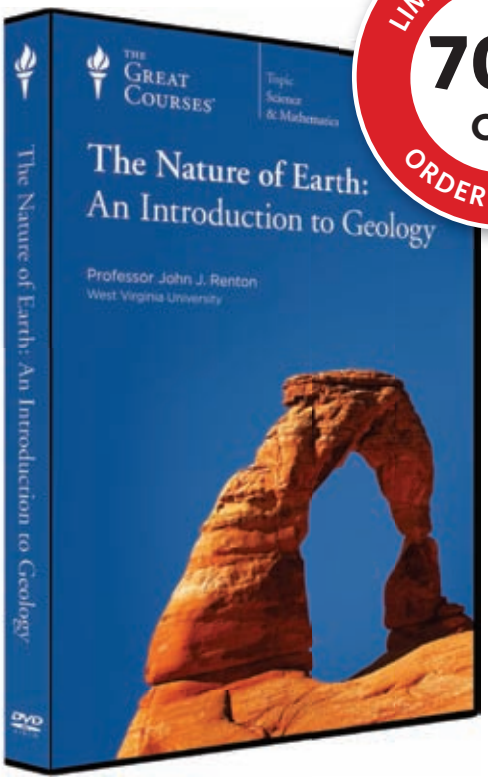

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INFECTIOUS DISEASE

Outsmarting Dengue Fever

Why one scientist is vaccinating mosquitoes, not patients

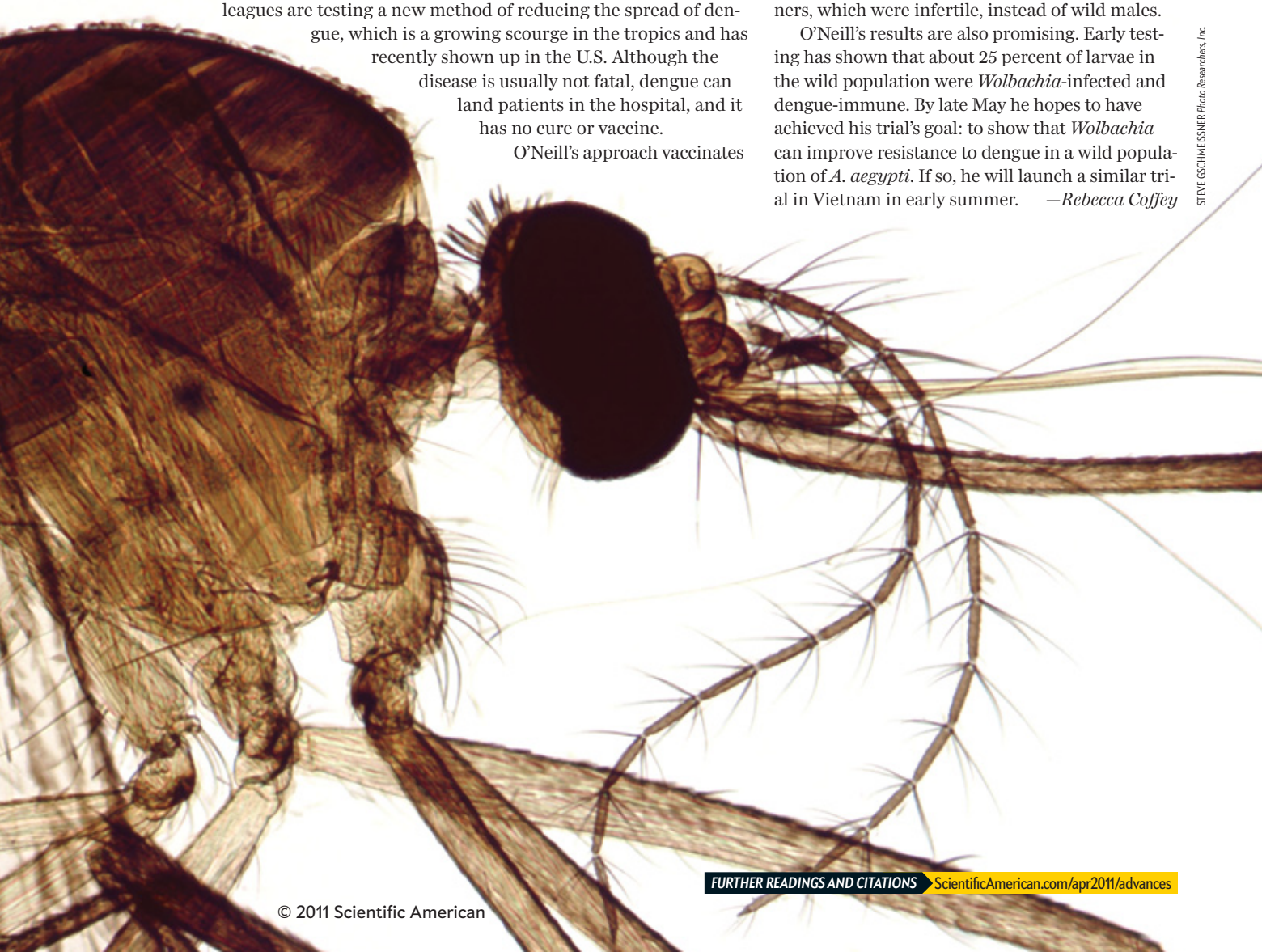
Just after sunrise in early January, a delivery van trundled along a suburban street in Queensland, Australia. Inside were tubs filled with a type of mosquito that carries dengue fever, the flulike illness that annually sickens 50 million to 100 million people worldwide. Workers inside the van stopped at every fourth house, took out what resembled a small Chinese food container and released 40 mosquitoes into the wild. After a week, they had filled the air with 6,000 insects. By early March they had launched 72,000.

What may sound like bioterrorism is, in fact, a novel form of biological insect control. Scott O'Neill of the University of Queensland and his colleagues are testing a new method of reducing the spread of dengue, which is a growing scourge in the tropics and has recently shown up in the U.S. Although the disease is usually not fatal, dengue can land patients in the hospital, and it has no cure or vaccine.

O'Neill's approach vaccinates mosquitoes instead of patients. In his lab, under a microscope, workers inject the bacterium *Wolbachia pipientis,* which is harmless to humans and common among insects, into eggs of *Aedes aegypti* mosquitoes, a major carrier of the dengue microbe. O'Neill has found that *Wolbachia* makes *A. aegypti* resistant to—and unable to transmit—the disease. What is more, all progeny inherit immunity.

O'Neill's method, which entails no genetic modification, stands in contrast to dengue-control efforts that made headlines this past winter. In December, British biotechnology company Oxitec released 6,000 genetically modified male mosquitoes in Malaysia to the alarm of some groups that expressed concern about the possible effects of GM insects on humans and ecosystems. Results are not yet available for Malaysia, but Luke Alphey, chief scientist and founder of Oxitec, says an earlier release of 3.3 million of the mosquitoes on Grand Cayman Island resulted in an 80 percent reduction in *A. aegypti,* presumably because many females ended up mating with GM partners, which were infertile, instead of wild males.

O'Neill's results are also promising. Early testing has shown that about 25 percent of larvae in the wild population were *Wolbachia*-infected and dengue-immune. By late May he hopes to have achieved his trial's goal: to show that *Wolbachia* can improve resistance to dengue in a wild population of *A. aegypti*. If so, he will launch a similar trial in Vietnam in early summer. —*Rebecca Coffey*



STEVE GSCHMEISSNER *Photo Researchers, Inc.*

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ARE YOU KIDDING YOURSELF?

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Lipitor is backed by over 18 years of research.

Talk to your doctor about your risk and about Lipitor. Learn more at lipitor.com or call 1-888-LIPITOR (1-888-547-4867).

Please see additional important information on next page.

IMPORTANT SAFETY INFORMATION:
LIPITOR is not for everyone. It is not for those with liver problems. And it is not for women who are nursing, pregnant or may become pregnant.

If you take LIPITOR, tell your doctor if you feel any new muscle pain or weakness. This could be a sign of rare but serious muscle side effects. Tell your doctor about all medications you take. This may help avoid serious drug interactions. Your doctor should do blood tests to check your liver function before and during treatment and may adjust your dose.

Common side effects are diarrhea, upset stomach, muscle and joint pain, and changes in some blood tests.

INDICATION:
LIPITOR is a prescription medicine that is used along with a low-fat diet. It lowers the LDL ("bad" cholesterol) and triglycerides in your blood. It can raise your HDL ("good" cholesterol) as well. LIPITOR can lower the risk for heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as age, smoking, high blood pressure, low HDL, or family history of early heart disease.

LIPITOR can lower the risk for heart attack or stroke in patients with diabetes and risk factors such as diabetic eye or kidney problems, smoking or high blood pressure.

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High cholesterol is more than just a number, it's a risk factor that should not be ignored. If your doctor said you have high cholesterol, you may be at an increased risk for heart attack and stroke. But the good news is, you can take steps to lower your cholesterol.

With the help of your doctor and a cholesterol-lowering medicine like LIPITOR, along with diet and exercise, you could be on your way to lowering your cholesterol.

Ready to start eating right and exercising more? Talk to your doctor and visit the American Heart Association at www.americanheart.org.

WHO IS LIPITOR FOR?

Who can take LIPITOR:

- People who cannot lower their cholesterol enough with diet and exercise
- Adults and children over 10

Who should NOT take LIPITOR:

- Women who are pregnant, may be pregnant, or may become pregnant. LIPITOR may harm your unborn baby. If you become pregnant, stop LIPITOR and call your doctor right away.
- Women who are breast-feeding. LIPITOR can pass into your breast milk and may harm your baby.
- People with liver problems
- People allergic to anything in LIPITOR

BEFORE YOU START LIPITOR

Tell your doctor:

- About all medications you take, including prescriptions, over-the-counter medications, vitamins, and herbal supplements
- If you have muscle aches or weakness
- If you drink more than 2 alcoholic drinks a day
- If you have diabetes or kidney problems
- If you have a thyroid problem

ABOUT LIPITOR

LIPITOR is a prescription medicine. Along with diet and exercise, it lowers "bad" cholesterol in your blood. It can also raise "good" cholesterol (HDL-C).

LIPITOR can lower the risk of heart attack, stroke, certain types of heart surgery, and chest pain in patients who have heart disease or risk factors for heart disease such as:

- age, smoking, high blood pressure, low HDL-C, family history of early heart disease

LIPITOR can lower the risk of heart attack or stroke in patients with diabetes and risk factors such as diabetic eye or kidney problems, smoking, or high blood pressure.

POSSIBLE SIDE EFFECTS OF LIPITOR

Serious side effects in a small number of people:

- **Muscle problems** that can lead to kidney problems, including kidney failure. Your chance for muscle problems is higher if you take certain other medicines with LIPITOR.
- **Liver problems**. Your doctor may do blood tests to check your liver before you start LIPITOR and while you are taking it.

Call your doctor right away if you have:

- Unexplained muscle weakness or pain, especially if you have a fever or feel very tired
- Allergic reactions including swelling of the face, lips, tongue, and/or throat that may cause difficulty in breathing or swallowing which may require treatment right away
- Nausea, vomiting, or stomach pain
- Brown or dark-colored urine
- Feeling more tired than usual
- Your skin and the whites of your eyes turn yellow
- Allergic skin reactions

Common side effects of LIPITOR are:

- Diarrhea
- Upset stomach
- Muscle and joint pain
- Changes in some blood tests

HOW TO TAKE LIPITOR

Do:

- Take LIPITOR as prescribed by your doctor.
- Try to eat heart-healthy foods while you take LIPITOR.
- Take LIPITOR at any time of day, with or without food.
- If you miss a dose, take it as soon as you remember. But if it has been more than 12 hours since your missed dose, wait. Take the next dose at your regular time.

Don't:

- Do not change or stop your dose before talking to your doctor.
- Do not start new medicines before talking to your doctor.
- Do not give your LIPITOR to other people. It may harm them even if your problems are the same.
- Do not break the tablet.

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CHILD PSYCHOLOGY

Tame Your Inner Tiger

Controlling parents tend to have children who are academically above average but depressed

All parents struggle to find the right balance between encouragement and discipline when it comes to raising their kids. This past winter Yale University law professor Amy Chua drew roars of protest when she asserted in her book, *Battle Hymn of the Tiger Mother,* that successful parenting entails controlling most aspects of a child's life, from prohibiting playdates and sleepovers to screaming at children for getting grades lower than an A. What does research say about this style of child-rearing?

"There's no evidence that intrusiveness is appropriate in any culture we've been to before, including China," says psychologist Brian K. Barber of the University of Tennessee Knoxville. To learn more about how psychological control might vary across the world, Barber and his colleagues interviewed 120 adolescents from five different cultures, including Costa Rica, Thailand and South Africa, and then surveyed another 2,100. Their findings, which they recently submitted to the *Journal of Adolescence,* suggest that some of the behavior described in Chua's book, such as insulting kids (she once called her daughter "garbage"), invalidating their feelings and violating their privacy, correlated with children's depression and antisocial behavior, a finding that matches past research.

Barber distinguishes "authoritarian" households—those that are overly coercive—from "authoritative" households, where strictness is accompanied by warmth and encouragement of self-direction. In a prior study of more than 20,000 U.S. high schoolers, Laurence Steinberg of Temple University and his colleagues found that children raised in authoritative households were typically psychologically healthy, whereas those raised in authoritarian ones had elevated anxiety and depression. Notably kids from both households got comparably good grades, suggesting tiger mothering isn't necessary for excellence after all. *—Charles Q. Choi*

BEN HIDER *Getty Images (game show)*

COMPUTER SCIENCE

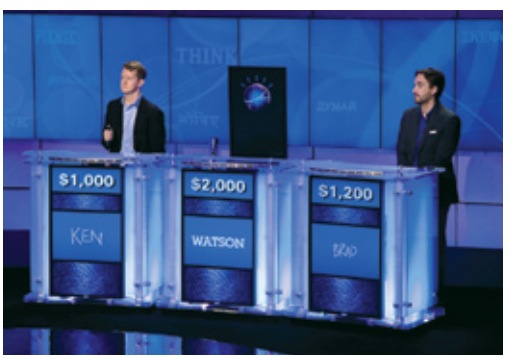
Watson Looks for Work

What's next for the artificially intelligent *Jeopardy* champion?

A team of IBM researchers spent four years building Watson, a computer system clever enough to beat the best *Jeopardy* players in the world. And although the three-day competition marked the end of Watson's game-show career, it was just the beginning of Watson's life in business.

One of the things that makes Watson unique is its ability to understand natural language—"getting at the meaning of words and understanding what humans meant, not just what they said or wrote," says Katharine Frase, IBM's vice president of research. On *Jeopardy* this means being able to pick through a riddle of a quiz-show clue; in the corporate world it could be used to decipher the needs of a customer. For example, callers to a help desk often "don't describe the problem in a language that the person on the other end of the phone understands," Frase says. A Watson-like system would act as a translation tool, turning English into engineerese.

Once Watson knows what is being asked, it must find the answer. The system that appeared on *Jeopardy* was preloaded with 200 million pages of encyclopedias, newspapers and works of literature. Any *Jeopardy* champion has absorbed a good deal of this material over the course of a curious life. But consider the medical literature, where "there's so much information it seems almost inhuman to ask a doctor to be up to speed," Frase says. This makes it perfect for the extremely inhuman Watson. One of IBM's first projects will be to develop a system that would allow a small-town doctor to investigate a strange constellation of symptoms. From here it is easy to imagine a machine built for law or finance, one loaded with every legal decision handed down by the courts or the full text of every financial document published by every publicly traded entity in the world.



But one thing Watson can't help with is deciding what projects to prioritize. "At this point the hardest problem is figuring out all the things we could do and what we should do," Frase says. The company hopes to build prototype systems by the end of the year. After four years of education, Watson has passed its final exam; now it's time to go find a job.

—Michael Moyer

BY THE NUMBERS

$53 billion

President Barack Obama's proposed funding for high-speed-rail expansion between 2012 and 2017, which he submitted as part of his 2012 budget in February.

$451 billion: China's planned minimum spending on high-speed-rail expansion between 2011 and 2015.

Illustrations by Thomas Fuchs

Accelerating Software Modernization
with Artificial Intelligence

AI is radically transforming the way organizations evolve their software assets to achieve competitive advantage.

Artificial Intelligence (AI) is the quest to achieve computers that equal or exceed human performance on complex intellectual tasks. A phenomenal development in AI is the recent emergence of automated computer language translation programs, driven by the need to modernize the nearly half trillion lines of legacy software developed during the latter half of the 20th century.

Early software translators of the 1990s, like the earliest chess programs, were disappointing and limited. Leveraging AI technologies that evolved from the 1980s era USAF's Knowledge Based Software Assistant and emerging standards, computers can now understand and translate software applications with levels of proficiency that vastly exceed human performance. This technology is revolutionizing the way industries, such as finance, insurance, manufacturing, and healthcare as well as military and governments are modernizing their legacy systems.

Leading this field is The Software Revolution, Inc. (TSRI), a Kirkland, Washington based company. Building upon 32 years of continuous R&D, TSRI's robust *JANUS* Studio® tool suite provides large-scale, error-free legacy system modernizations at 100% levels of automation. By applying AI to abstract software models, TSRI delivers automated code conversion with unprecedented target code quality, economies of scale and schedule compression, accomplishing with small teams in months what would take years by other means. The following list of brief case studies represents five recent TSRI legacy system modernization projects.

• **European Air Traffic Management System (EATMS), Thales Air Systems:** This realtime system manages over 10 million passenger flights annually. Thales engaged TSRI to transform EUROCAT's 2 million lines of legacy Ada into Java. The result was a perfect functional replica of EUROCAT in its new language. TSRI's 100% automation eliminated the risk of errors inherent in a manual rewrite. EUROCAT will commence operation in significant airports across Europe and Asia at the end of 2011.

• **Patriot Missile, Fire Platoon Simulation & Battalion Simulation Support Systems, Raytheon:** TSRI used the *JANUS* Studio® tool suite to modernize four different Patriot systems including Patriot Japan. These modernizations included the transformation of nearly 200 thousand source lines of Fortran code to C++, re-factoring and documentation.

• **Major Healthcare Insurance Company:** This system consisted of over 180 thousand source lines of PowerBuilder and nearly 3 million lines of COBOL. In modernizing this system TSRI provided transformation, re-factoring and supported system integration. This project was completed in only 15 months.

• **Major US Bank:** This legacy application contained over 3 million source lines of Fortran and over 160 thousand lines of DCL. TSRI automatically generated a *Transformation Blueprint*™ to assist in the systems design architecture, performed the code documentation and provided engineering support.

• **Advanced Field Artillery Tactical Data System (AFATDS), Stanley and Associates (Now CGI Federal):** A version of the US Army's legacy AFATDS system consisting of over 5 million source lines of ADA-83. TSRI employed *JANUS* Studio® to transform this system into Java in only 10 months. TSRI delivered the modern system to Stanley in August 2010.

Information Systems Transformation: *Architecture-Driven Modernization Case Studies* provides more detailed information on these case studies.

For more information visit www.tsri.com

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By William M. Ulrich and Philip Newcomb
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Mr. Newcomb is an internationally recognized expert in the application of AI and formal methods to software engineering. After leaving Boeing he led a team of software engineers to develop TSRI's *JANUS* Studio® tool suite. Mr. Newcomb is the author of numerous papers, books and industry standards.

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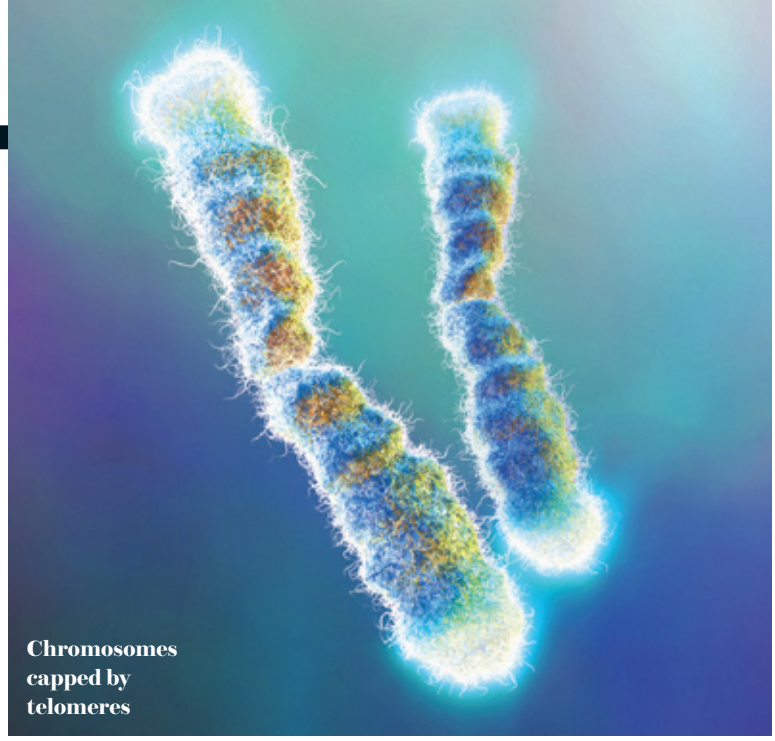

Chromosomes capped by telomeres

HEALTH

My, What Long Telomeres You Have

Researchers will soon be offering a simple test that aims to tell patients how quickly they are aging

Doctors routinely urge their patients to quit smoking and exercise regularly. But what if there were a blood test that could show smokers and couch potatoes the damage their lifestyle was actually wreaking on their chromosomes?

Two groups of prominent researchers have started companies to provide just such a test, which would measure the length of one's telomeres. Telomeres are caps on the ends of chromosomes, protecting them much as plastic tips on the ends of shoelaces keep the laces from fraying. Whenever chromosomes—the storehouses of our genes—are replicated in preparation for cell division, their telomeres shorten. That shrinking has led many scientists to view telomere length as a marker of biological aging, a "molecular" clock ticking off the cell's life span, as well as an indicator of overall health. Studies comparing the telomere length of white blood cells among groups of volunteers show distinct correlations between telomere length and lifestyle. Those who exercise regularly have longer telomeres than those who do not. Folks who perceive themselves as the most stressed have shorter telomeres than those who see themselves as the least. Certain diseases, too, correlate with shorter telomeres, including cardiovascular, obesity and Alzheimer's.

"Knowing whether our telomeres are a normal length or not for a given chronological age will give us an indication of our health status and of our physiological 'age' even before diseases appear," says María A. Blasco, who heads the Telomeres and Telomerase Group at the Spanish National Cancer Research Center and who co-founded the company Life Length in September. Telomere research pioneer Calvin B. Harley, who co-founded Telome Health last spring with Nobel laureate Elizabeth H. Blackburn, considers telomere length "probably the best single measure of our integrated genetics, previous lifestyle and environmental exposures." Beginning as early as this spring, the companies will offer telomere-measurement tests to research centers and companies studying the role of telomeres in aging and disease; the general public may have access by the fall through doctors and laboratories, perhaps even directly.

Although enthusiasm for the research services runs high, some telomere experts question the tests' current value for individuals. "We haven't defined what we consider to be a norm and what we consider to be abnormal, either long or short," says Nilesh J. Samani, head of cardiovascular services at the University of Leicester in England. But telomere length is not a diagnosis or a prognosis, Harley says. The data, he insists, *are* sufficient to help people make "personal lifestyle decisions," regarding, say, diet, exercise and stress.

—Thea Singer

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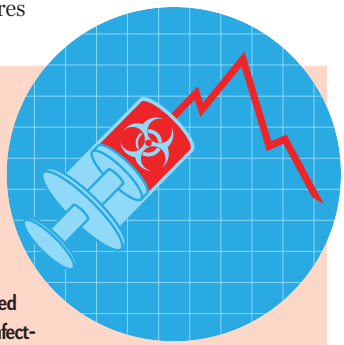
ECONOMICS

Too Contagious to Fail

Why bankers should think more like epidemiologists



What could the study of infectious disease teach us about the 2008 financial crisis? Plenty, argue University of Oxford ecologist Robert M. May and Andrew G. Haldane, the Bank of England's executive director for financial stability. In a recent paper they compared big banks such as Lehman Brothers with what epidemiologists call "superspreaders"—infected people or organisms who endanger entire networks through their web of connections.

To prevent another meltdown, financial regulators may need to focus on the health of networks, not just individual banks, May notes. In focusing on interconnections, bankers would be following the lead of designers of personal computers and utility grids; all have worked to make their systems modular, creating firewalls to prevent infection of the whole network by a single element in it. Says Philip H. Dybvig, an economist at Washington University in St. Louis: "What they're proposing is really a version of Glass-Steagall," an act that separated investment banks from commercial ones, revoked in 1999. Are bankers listening? May cites the U.S.'s recently proposed Volcker rule—which suggested quarantining risky hedge fund and private equity activity from other banking activities—as a sign that they may be thinking more like epidemiologists.

—Carla Power

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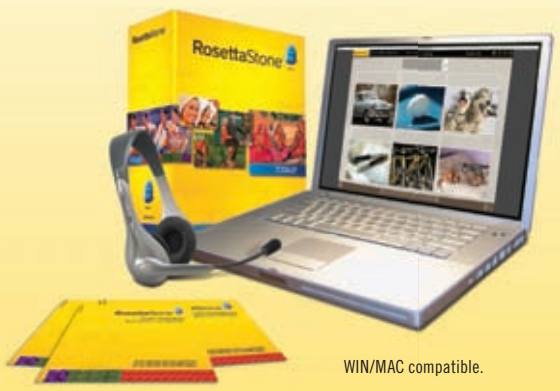

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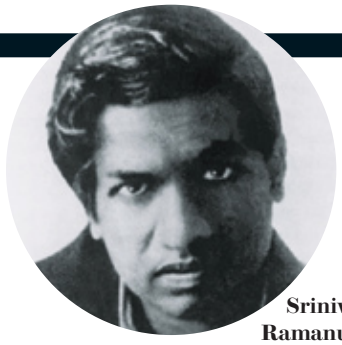
Cracking a Century-Old Enigma

Mathematicians unearth fractal counting patterns to explain a cryptic claim



Srinivasa Ramanujan

For someone who died at the age of 32, the largely self-taught Indian mathematician Srinivasa Ramanujan left behind an impressive legacy. Number theorists have now finally managed to make sense of one of his more enigmatic statements, written just one year before his death in 1920.

The statement concerned the deceptively simple concept of partitions. Partitions are subdivisions of a whole number into smaller ones. For example, for the number 5 there are seven options:

$5 \cdot 1+1+1+1+1 \cdot 1+1+1+2$
$1+1+3 \cdot 1+2+2 \cdot 1+4 \cdot 2+3$

Mathematicians express this by saying $p(5) = 7$. For the number 6 there are 11 possibilities: $p(6) = 11$. As the number n increases, the partition number $p(n)$ soon starts to grow very fast: for example, $p(100) = 190{,}569{,}292$, and $p(1{,}000)$ is a 32-figure number.

For centuries mathematicians have struggled to make sense of partitions, in part by hunting for patterns that link them together. Ramanujan noticed that if you started with the number 9 and kept adding 5's to that number, the partitions would all be divisible by 5. For example: $p(9) = 30$, $p(9 + 5) = 135$, $p(9 + 10) = 490$, and $p(9 + 15) = 1{,}575$. He posited that this pattern should go on forever and that similar patterns exist when 5 is replaced by 7 or 11, the next two prime numbers (primes are numbers that are divisible only by themselves or by 1), and also by *powers* of 5, 7 or 11. Thus, for instance, there should be an infinity of n's at intervals of 5^3 such that all the corresponding $p(n)$'s should be divisible by 125. Then, in a nearly oracular tone, Ramanujan wrote that there should be no corresponding "simple properties" involving larger primes—in other words, there is no sequence of $p(n)$'s that are all divisible by 13, 17 or 19 and so on. In the years since, researchers have looked fruitlessly for patterns linking these higher primes.

In January, Ken Ono of Emory University and his collaborators finally found a solution: they described for the first time formulas linking n's that come at intervals of the powers of 13 (13, 13^2, 13^3 …) and of the higher primes. The formulas are not "simple," in the sense that they do not say that the $p(n)$'s are divisible by powers of 13; instead they reveal relations among the *remainders* of such divisions. For each prime, as the exponent grows, the formulas recur in ways that are reminiscent of fractals—structures in which patterns or shapes repeat identically at multiple different scales.

In a separate result also announced in January, Ono and another collaborator described the first formula that directly calculates $p(n)$ for any n, a feat that had eluded number theorists for centuries.

Will the new discoveries have any practical use? Hard to predict, says George E. Andrews of Pennsylvania State University. "Deep understanding of underlying pure mathematics may take a while to filter into applications."

—*Davide Castelvecchi*

QUOTABLE

"Science unleavened by the human heart and the human spirit is sterile, cold and self-absorbed."

—Brandeis University biochemist Gregory A. Petsko on the University of Albany's decision to cut humanities programs due to budget cuts. His letter was the most viewed paper on biomedcentral.com in the last year.

PHOTO RESEARCHERS, INC.

COMMENT AT ScientificAmerican.com/apr2011

KEVIN MACKENZIE *University of Aberdeen*

WHAT IS IT?

Smaller fleas: *What appears as a mere speck to the human eye has plenty of character when observed under a microscope. The nearly invisible* Daphnia, *a water flea, came to life with tufts of hair, big eyes and red "lips" when magnified 50 times. Kevin Mackenzie, manager of the University of Aberdeen's Microscopy and Imaging Facility in Scotland, photographed this two-millimeter pond invertebrate whose wispy hair is actually a pair of antennae. The beauty mark below its compound eye* (black) *is a light-sensing organ called an ocellus. The flea's transparent body also reveals its last meal: algae* (green).

In February scientists reported sequencing the genome of a Daphnia *species,* D. pulex, *for the first time. The sequence will help researchers study how the environment influences the functions of genes, says project leader John Colbourne of Indiana University. Municipalities have long monitored* Daphnia *population sizes for signs of water pollution, because the critter is extremely sensitive to it. Looking at alterations in gene behavior, he notes, can also provide new clues to how chemicals might affect human health.* —Ann Chin

AGRICULTURE

Arid Land, Thirsty Crops

Two techniques show promise for helping farmers conserve scarce water in Punjab, India's breadbasket

India is running out of water for crops. Most of the water-intensive agriculture in the nation takes place in Punjab, a state in the northwest that makes up 2 percent of the country's territory but provides more than 50 percent of its grain reserves. Farmers there currently pump out 45 percent more groundwater than is replenished by monsoon rains.

The problem has arisen in part because Punjabi farmers have veered away from growing traditional crops that are suited for semiarid land, such as wheat and corn, and turned instead to more profitable, but water-intensive, rice. "If Punjab is to continue as the food grain capital of India, modern agricultural practices will have to take into account the water situation and create a feasible long-range plan for a sustainable future," says Shama Perveen, an associate research scientist at Columbia University's Water Center, who has been working in the region. She and several colleagues from Columbia, in collaboration with Indian agriculture scientists, are testing a piece of that plan: two conservation tools that could help farmers use less water, even if it won't alter their choice of crops.

One such tool is the tensiometer: a porous, ceramic bulb attached to a color-coded meter that reflects the moisture content of soil. In a preliminary experiment involving more than 500 farmers in 50 Punjab villages, the group handed out tensiometers, which were stuck into fields, including rice paddies. Farmers were told to irrigate the land only when the instruments showed that the moisture content was falling. Those who followed that guideline consumed nearly 30 percent less water than before.

The other technique relies on lasers that detect undulations in fields. Informed by the laser scans, farmers can level out any detected bumps before sowing, to help prevent puddles and dry patches and allow for more uniform irrigation. Laser leveling can save up to 20 percent of water usage, says Kapil Narula, head of the Columbia Water Center's India operations.

Later this year the team will introduce tensiometers and laser leveling to 5,000 more farmers in Punjab and to 1,500 farmers in the nearby state of Gujarat. "By involving greater numbers of farmers, we can effectively address the water crisis at least in acutely felt areas," Narula says.

Local experts are encouraged by the results but say they need to be scaled up and combined with other efforts to have a substantial effect. "The challenge is to involve larger numbers of farmers and to educate them about [the tools'] efficacy," says Bhishm Kumar, a scientist at the National Institute of Hydrology at Roorkee. He adds that scientists and farmers need to apply multiple approaches to deal with the crisis, including planting crops that require less water and introducing modern drip irrigation, which funnels water directly to the roots of plants. —*Sudip Mazumdar*

Drought mentality: A farmer in Punjab examines what is left of his crop during a dry period.

AJAY VERMA *Reuters*

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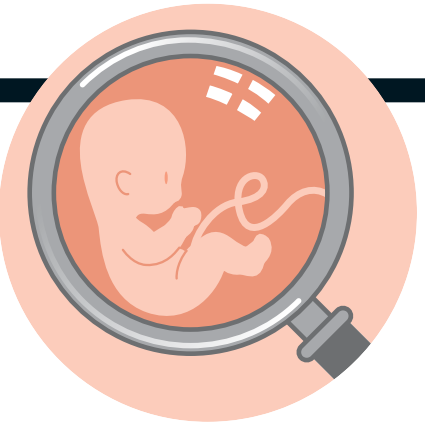
GENETICS

Too Much Information?

A series of recent breakthroughs means that early, noninvasive genetic tests for fetuses may be just two years away



Today expectant parents concerned about the diseases that could afflict their unborn children don't have a lot of options. Blood tests can determine whether parents carry mutations for such genetic diseases as cystic fibrosis and Tay-Sachs, but they can't determine whether the baby will inherit them. And although fetuses can be tested for Down syndrome and other chromosomal abnormalities using amniocentesis or chorionic villus sampling, about 1 percent of procedures cause miscarriage, so many moms opt out. But thanks to a handful of recent breakthroughs, noninvasive prenatal tests may soon be available that diagnose genetic diseases before birth using samples of a mother's blood—an exciting possibility that also raises difficult questions about how they should be regulated and administered.

What makes noninvasive tests possible is that a pregnant woman's blood contains free-floating copies of her fetus's genes, as chemical pathologist Dennis Lo of the Chinese University of Hong Kong discovered in 1997. Last December in *Science Translational Medicine,* Lo reported on a method of sequencing individual fetal genes and counting individual fetal chromosomes in a mother's blood to establish whether a fetus carries disease-causing mutations or chromosomal abnormalities. Fetal genes inherited from the mother are identifiable because they are present in higher-than-normal concentrations in the mother's blood; gene variants not shared by the mother are assumed to be inherited from the father. In a follow-up article in the *British Medical Journal,* Lo tested his approach on 753 pregnant women. He counted the proportion of DNA molecules found in the mother's blood that were derived from chromosome 21—individuals with Down syndrome have three copies rather than the normal two—and accurately diagnosed 100 percent of the fetuses who would be born with the disorder. The test, Lo says, would prevent "98 percent of invasive procedures, such as amniocentesis." The trial did, however, report three false positives, so all positive results would need to be followed up with more invasive tests.

San Diego company Sequenom is developing a test based on Lo's method that should be available within two years. Tests for other conditions, including cystic fibrosis, Tay-Sachs, hemophilia and sickle cell disease, may be four to five years away.

The big question is how these tests will affect parental decisions: Will couples abort affected fetuses? How will the prevention of rare diseases affect research funding for their cures? Will tests arise that allow parents to select fetuses based on superficial traits, such as eye or hair color? Stanford University law professor Henry T. Greely says that the U.S. government is doing nothing to address these questions. In addition, doctors will need guidelines to help them counsel test takers properly. Otherwise "you will end up with families getting information they're not ready to get," says Siobhan Dolan, an obstetrician at Montefiore Medical Center in New York. In a few years, we might have too many options rather than too few. —*Melinda Wenner Moyer*

BY THE NUMBERS

225 miles

Current length of the U.S.'s only high-speed-rail line, part of the Acela Express, which debuted in 2000.

2,594 miles: Current length of China's high-speed-rail system.

4,124 miles: Current length of high-speed-rail systems in Europe.

FIELD NOTES

Getting to Know You

The brain behind many of the shortened URLs on the Web talks about data analysis and how it lets her figure out which soccer team won without watching the match

PROFILE

NAME
Hilary Mason

TITLE
Chief scientist, bit.ly

LOCATION
New York City

I joined bit.ly as chief scientist in October of 2009. The company is a URL-shortener and content-sharing platform; we provide tools for people to share and track links on the Internet.

People might not imagine that there are scientists working at Internet start-ups, but bit.ly was a bit ahead of the trend of recognizing the value of data. Approximately one third of my day is spent doing pure research—looking at data about what people click on, trying to figure out what it says about human behavior and communication. I look for interesting events, trends or visualizations. During the World Cup, for example, we could determine what two teams were playing and what team won without even watching the game—during the games the people in the two competing countries would be clicking on soccer links. After the game, though, the people in the winning country would continue to click soccer links while the people in the losing country would not.

The other two thirds of my day I focus on translating models and equations into functional systems. Recently we built a program that takes a link you're interested in and spits back similar links. It's great for finding different perspectives on the same topic. In our current project we're developing a social newsreader that learns your interests and recommends links in real time. After that, we'd like to provide contextually aware information. So if you're a pizza lover in New York City, we'd let you know right away if a famous pizza place nearby is having a special.

After graduate school, I joined Johnson & Wales University in Rhode Island as an assistant professor, but I continued to program in addition to teaching and working on research. I built a program that crawled job boards to determine which skills employers value, which helped Johnson & Wales explore ways to improve its curriculum.

Projects like that made me realize that I wanted mainly to code and build useful things, so I left teaching.

I'm really curious about people—what their desires and interests are—and bit.ly's data tell me that. It gives me an unprecedented window into human communication and behavior.

—As told to Michael Easter

PINAR ÖZGER

QUOTABLE

"One beaten man is worth two unbeaten men."

—Russian prime minister Vladimir Putin, referring to BP, which just signed an Arctic exploration deal with Russia. Putin meant that BP, having learned its lesson during the Gulf oil spill, has emerged as a safer company.

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INGO ARNDT *Minden Pictures*

MARINE BIOLOGY

Crab Love Nest

A researcher spent 10 years learning what makes horseshoe crabs mate

Carmela Cuomo thought she had the secret within reach, hidden in a shallow black tank at the NOAA marine fisheries laboratory in Milford, Conn. The horseshoe crabs she had plucked from New Haven Harbor in 2000 trundled about their springtime ritual, digging pits in the sand, laying their eggs and fertilizing them. She was trying to understand what formula of light, food and chemistry induced these 500-million-year-old creatures to breed. But the next year, before she could figure it out, the crabs stopped mating, and the secret eluded her.

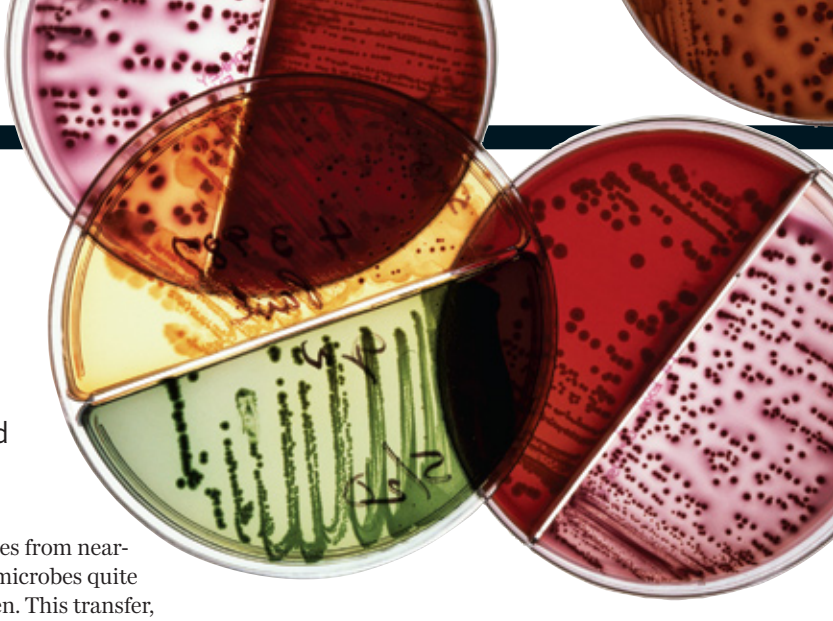
Cuomo, an environmental scientist at the University of New Haven, continued to search for the answer for 10 years, in the tanks at Milford, at labs at her university, and in a set of aquariums in her own basement. Now, finally, she has begun to unlock the mystery.

Having the answer would have major practical implications. No one, except by accident, has been able to get horseshoe crabs to mate in captivity. If scientists could figure out how to breed them, the ability might take pressure off the wild populations along the U.S. Atlantic coast and in East Asia. The pharmaceutical and medical products industries value the armored arthropods because a clotting extract from their blood is the world standard for detecting deadly gram-negative bacteria. Their eggs are also a vital food source for migrating shorebirds. And a huge fishing industry uses them for bait.

When Cuomo's crabs failed to mate in 2001, she fiddled with mimicking the tides, altered the angle of her artificial beaches, and changed their food. Each year she shifted her parameters, but nothing worked. Then, in 2007, at an international conference on horseshoe crabs, Cuomo heard an elderly Japanese researcher talk about raising crabs in mud taken from the beach where the eggs were laid. Cuomo realized what had been missing from her breeding experiment: natal sand. The one year she had managed to get her crabs to breed, unlike any other year, she had taken both the crabs and the sand for her tanks from the same spot. She tried again, and the crabs canoodled—not only in the traditional late spring season, but ongoing into October. She has repeated the process, with the same success.

Now, driven by her innate curiosity, Cuomo is moving on to other aspects of the mystery: What's in the sand that matters? How do the crabs sense it? And can she help save a species?

—David Funkhouser



MICROBIOLOGY

To Share and Share Alike

Bacteria swap genes with their neighbors more frequently than researchers have realized

Bacteria and archaea—collectively known as prokaryotes—live pretty much everywhere, dividing happily in places from stomach acid to deep-sea vents. They can thrive in so many different places because their genomes are incredibly flexible: they can alter, lose and duplicate genes almost at will. Scientists have long recognized that prokaryotes can also acquire genes from their neighbors (a move that contributes to antibiotic resistance). But this method of gaining new DNA, termed horizontal gene transfer, was thought to be relatively rare and to occur only under strong pressures in the environment, such as exposure to powerful antibiotics.

A recent study in *PLoS Genetics* has found, instead, that prokaryotes acquire genes from nearby microbes quite often. This transfer, which can take place when one bug obtains genetic information from another via a bridge or a virus, can happen even when the two prokaryotes are from different species.

By compiling a database of 110 different prokaryote genomes, Todd J. Treangen and Eduardo P. C. Rocha of the Pasteur Institute in Paris calculated the number of genes that had been acquired through horizontal gene transfer. They knew that genes that evolve within a prokaryote's own genome are often located near similar genes and have similar functions in existing genes. Genes that arrive via horizontal transfer, however, appear randomly throughout the genome and often have radically different functions. By tracking these two major markers, Treangen and Rocha calculated that the

WALTER HODGES *Corbis*

COMMENT AT ScientificAmerican.com/apr2011

prokaryotes they studied acquired between 88 and 98 percent of new genes through horizontal transfer.

"This [study] shows that most new genes in bacteria are gained from outside sources," says Howard Ochman, a microbiologist at Yale University, who was not involved in the research. "It took full genome sequences and a lot of good sense about how to cull the data, and I think that their conclusions are really robust."

After arriving in their new homes, transferred genes follow a different evolutionary path than do genes that evolve within the same genome. The newcomers evolve more quickly and stay longer—behaviors that Treangen suspects arise because the genes provide radical new and useful functionality.

Horizontal gene transfer allows prokaryotes to acquire "preexisting adaptations from other microbes," says Treangen, which enables them to rapidly establish themselves in new environments. This study, he asserts, shows that horizontal transfer is the dominant force driving prokaryote evolution and helps to explain why bacteria have developed antibiotic resistance so quickly.

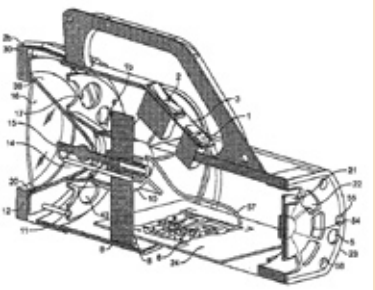
—Carrie Arnold

PATENT WATCH

Incapacitating light beam: *The suspect is going for his gun, and the police officer doesn't want to shoot. The founders of a company called Genesis Illumination hope police officers will soon be reaching for a StunRay instead of a gun or Taser. They claim their newly patented device can render an assailant helpless with a brief flash of high-intensity light. It works by overloading the neural networks connected to the retina, saturating the target's world in a blinding pool of white light. "It's the inverse of blindness—the technical term is a loss of contrast sensitivity," says Todd Eisenberg, the engineer who invented the device. "The typical response is for the person to freeze. Law enforcement can easily walk up and apprehend [the suspect]."*

The device consists of a 75-watt lamp, combined with optics that collect and focus the visible light into a targeted beam, which can be aimed like a flashlight. Recovery time ranges from "seconds to 20 minutes," Eisenberg says. "It's very analogous to walking from a very bright room into a very dark room."

The inventors say the StunRay has a number of advantages over taser guns, which work best within a range of 12 to 15 feet. The StunRay can be effective from as far away as 150 feet. And whereas Tasers can cause cardiac arrest, the StunRay is reasonably safe. One downside is that the target must be facing the light for it to work. But "if the target has turned and is running away, the objectives of stopping an aggressive behavior or avoiding a potentially lethal confrontation have still been met," Eisenberg notes. —Adam Piore



PATENT NO. 7,866,082

U.S. PATENT AND TRADEMARK OFFICE

Veronique Greenwood is a science writer who reports frequently on biology and health.

Why Are Asthma Rates Soaring?

Researchers once blamed a cleaner world. Now they are not so sure

Asthma rates have been surging around the globe over the past three decades, and for a long time researchers thought they had a good idea of what might be fueling the increase: the world we live in is just a little too clean. According to this notion—known as the hygiene hypothesis—exposure in early childhood to infectious agents programs the immune system to mount differing highly effective defenses against disease-causing viruses, bacteria and parasites. Better sanitary conditions deprive the immune system of this training, so that for reasons that are still unclear, the body pounces on harmless particles—such as dust and ragweed—as if they were deadly threats. The resulting allergic reaction leads to the classic signs of asthma: chronic inflammation or swelling of the airways and acute spasms of those passageways.

Or so the thinking went. Although a lot of data support the hygiene hypothesis for allergies, the same cannot be said for asthma. Contrary to expectations, asthma rates have skyrocketed in urban areas in the U.S. that are not particularly clean. Moreover, the big increase in asthma rates in developed countries did not kick off until the 1980s—well after general sanitary conditions in the richer parts of the world had improved. And some studies are beginning to show that far from protecting children from asthma, respiratory infections in early childhood may actually be a risk factor for it.

The collapse of the hygiene hypothesis as a general explanation for the startling jump in asthma rates has led physicians and scientists to a new realization: asthma is a much more complex condition than anyone had truly appreciated. Indeed, it may not be even be a single disease. Studies now suggest that only half of asthma cases have an allergic component.

The prevention and treatment implications are significant. If, for instance, it is true that allergy is not a fundamental cause of asthma in many people, then an alternative mix of treatments may be more effective for those individuals. To root out asthma's cause (or causes) and properly treat the burgeoning number of people who are affected—300 million globally at last count—scientists will have to come to grips with the biology of its various forms.

BALANCING ACT

The hygiene hypothesis was first described in 1989 by David P. Strachan, a British epidemiologist who was studying hay fever. The more children in a family, he noticed, the lower the rates of hay fever and eczema, an allergic skin condition. Children in large families tend to swap colds and other infections more often than children with fewer siblings. Could it be that increased exposure to pathogens from their many siblings was protecting children from large families against allergies?

Breathe deep: Research into varying causes of asthma may eventually lead to new ideas on how to manage the condition.

That same year Erika von Mutius, an epidemiologist at Munich University, was looking into the effect of air pollution on asthma in what was then East and West Germany. Children from dirtier East Germany, she was shocked to find, had dramatically less asthma than their West German counterparts living in cleaner, more modern circumstances. The East German children, unlike their Western counterparts, had spent more time in day care and thus had likely been exposed to many more viruses and bacteria. "That was astonishing," she recalls, and led to "a major shift" in thinking.

These findings sparked intense debate among scientists. What is it about unhygienic living that might protect against asthma? One of the more popular explanations in the following decades entailed a balance between the immune cells that are involved in the body's reaction to most viruses and bacteria and those that are involved in the reaction to most parasites and allergens. These two groups of cells produce chemicals that in-

AIR RABBIT Getty Images

hibit each other. Early-childhood exposure to bacteria and viruses would cause the infection-related cells to become active, keeping the allergy- and parasite-related cells in check. Without that interplay, the allergy-related cells would later become overreactive, starting an allergic chain reaction that became chronic and ended in constricted airways, asthmatic spasms and labored breathing.

INCONVENIENT FACTS

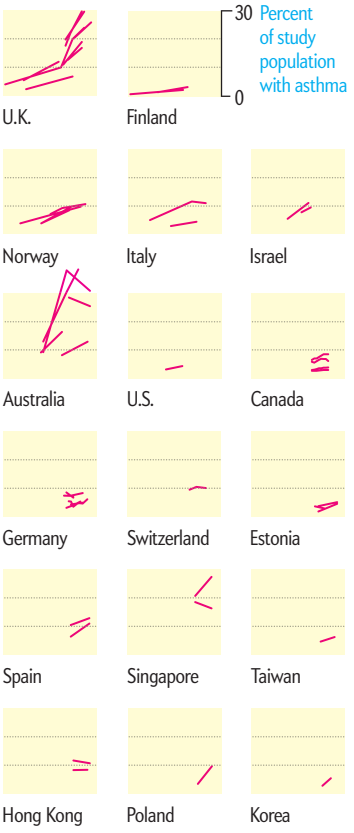
There was only one problem. As more data came in, they failed to tell the same story as the hygiene hypothesis. Children in Latin America with high rates of supposedly protective infection have even higher rates of asthma than children in western Europe. Inner-city children in Chicago and New York have quite high rates of asthma, despite unhygienic living. And the rates of asthma varied among countries with very similar histories of cleanliness—indicating that there was more to it than tidiness. For example, by 2004 Sweden's asthma cases had increased to 10 percent, according to one international study, while the number of cases in the U.K. had soared to 20 percent.

In addition, research showed that the relation between asthma and allergy is not at all straightforward. Some cases of asthma are indeed triggered by allergies, although the consensus among researchers over the past decade is that the connection is probably not as clear-cut as the hygiene hypothesis would suggest. Still other layers of immune regulation must be involved. Maria Yazdanbakhsh, a parasitologist at Leiden University in the Netherlands, has shown that people infected with parasitic worms have very high levels of the allergy-related immune cells but very low rates of asthma, disproving a direct connection between allergy and asthma in these cases at least.

What is more, a landmark review of asthma studies in 1999 by Neil Pearce, now at the London School of Hygiene and Tropical Medicine, demonstrated that at least half of asthma cases in the general population have no connection to allergic reactions at all. These could never be explained by the hygiene hypothesis.

In fact, the same factors that the hygiene hypothesis suggests protect people from developing allergic asthma may cause them to develop nonallergic asthma. "We think that dirt protects against allergic asthma, as foretold by the hygiene hypothesis, but increases the risk of having a nonallergic form," says Laura Rodrigues of the London School of Hygiene and Tropical Medicine, who studies asthma in Latin America. Pollutants in the air can irritate the airways and cause inflammation that leads to constricted breathing. Childhood colds, which the hygiene hypothesis suggested might help prevent development of asthma, can actually be a risk factor for asthma, especially if severe, says James E. Gern, a pediatrician who studies colds and asthma at the University of Wisconsin–Madison. "Early-life infections are an indicator of asthma risk rather than protective in any way," he says.

Changes in the Prevalence of Asthma, 1965–2005 (each line represents one study)



Global trends: Asthma rates are up around the world. But no one can explain why some countries, such as the U.K. and Australia, have seen greater jumps than others—or indeed why a few of the increases appear to be leveling off.

Besides the hygiene hypothesis, what can explain the increase in asthma rates? Other suggested causes include a rise in sedentary lifestyle, which could affect lung strength, and the rise in obesity, which increases inflammation throughout the body. A reworking of the hygiene hypothesis that focuses on changes in the normal nondisease-causing bacteria that live inside and on the body (in the intestines or the airways or on the skin) has promise. Studies by von Mutius and others have shown that children who live on farms where cows or pigs are raised and where they drink raw milk almost never have asthma, allergic or otherwise. Presumably because the children drank unpasteurized milk and handled livestock, they have different strains of normal bacteria in their airways that are somehow more protective than those found in city kids.

But the short answer to the question of why asthma has increased, according to Pearce, von Mutius, Rodrigues and many others, is, "We don't know." Pearce, in particular, wonders whether modernization in general or westernization in particular may play a role. "There is something about westernization that means people's immune systems function in a different way," he says. "But we don't know what the mechanism is."

Getting at the true underlying cause of the climb will require better ways of distinguishing among various possible types of asthma. Major asthma research networks supported by the National Institutes of Health have begun recording the details of thousands of individuals' symptoms and treatments. As the results are gathered and analyzed, researchers hope to identify clusters of asthma cases that have different causes and respond to different treatments. The hope is that "if you come in with these characteristics in asthma, we can anticipate what the prognosis is going to be and what the most effective treatment for you is going to be," says William W. Busse of the University of Wisconsin School of Medicine and Public Health, who is part of one such network.

It will take years to understand fully whether microbial exposure, lifestyle changes or the obesity epidemic is more important in explaining the continuing increase in asthma rates. But one thing is clear: the hygiene hypothesis was just the beginning. SA

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SOURCE: "THE ASTHMA EPIDEMIC," BY WALTRAUD EDER, MARKUS J. EGE AND ERIKA VON MUTIUS, IN *NEW ENGLAND JOURNAL OF MEDICINE*, VOL. 355, NO. 21; NOVEMBER 23, 2006

Graphic by Joshua Korenblat

David Pogue is the personal-technology columnist for the *New York Times* and an Emmy Award–winning correspondent for *CBS News*.

Seeing Forever

Digital photos and videos are great, but don't expect your grandkids to see them

Sooner or later every format goes digital. Audio recordings. Video recordings. TV signals. Photography. Books.

That's a wonderful thing, right? Digital means instant access. It means infinite duplication without loss of quality. It means instant transmission around the world. But unless we get diligent in a hurry, it could also mean a hit to our cultural record keeping.

Consider photographs, for example. We know what people looked like 150 years ago because the prints—yes, an analog format—are still around.

What photos does anybody print these days? Only a few special ones. We view the vast majority of digital photos on screens. That's convenient, they look great, and they're often much bigger than 4×6 prints. But will they be viewable in 50 years, let alone 150?

That would be assuming a lot. For one thing, it would assume that the JPEG format used by most digital photo files will still be around in 150 years. JPEG has a fighting chance, because there are so many billions of photo files, but it's not a sure thing. No computer format has been around for even 50 years.

The situation is even more grim when it comes to less mainstream files. Preserving video, for example, is going to be a nightmare. In the short history of digital camcorders, we've already accumulated a vast array of file types—MPEG-2, AVCHD, MiniDV, .MOV, .AVI, and so on—and that's not even counting the millions of dying tape formats they're stored on. What are the odds of these videos being playable in 50 years, let alone 100?

Already the current version of Microsoft Word can't open some documents from the first versions of the program. Do we really expect to be able to play AVCHD videos in 100 years?

Let's not even get into e-book formats. These book files (from Amazon, Barnes & Noble, Sony and Apple) are incompatible, proprietary, copy-protected—and brand-new. You really think that their copy-protection schemes or even the companies that invented them will still be around in 150 years?

No, when you buy a copy-protected book for your Kindle or Nook or iPad, you should assume that what you are buying is a temporary right to read—not the book itself. There's not much chance that you'll be passing your book collection down to your children or grandchildren, as you might with real books.

Whenever I write about format loss and data rot, a few enterprising companies always pipe up. "We've got a new Web site called EverStore—we'll store your digital files forever!" This is hilarious, considering that the Web as we know it isn't even 20 years old. Not a single online-storage company has been around for more than 10 years—and several have already gone out of business, including big-name services such as AOL's Xdrive. If you really think that the EverStores of today will keep your files safe for your grandchildren, well, here's a brochure for my Brooklyn Bridge Investment Trust.

In other words, in the rush to record humanity's stories in digital formats, it doesn't seem as though we are giving equal thought to how we are going to preserve them.

It's not hopeless, though. It's just going to require a lot of work. Prints from 100 years ago have reached us largely by accident; we may stumble upon caches of them in attics, for example. But in digital, nothing happens by accident. Nobody is going to stumble across the photos on your hard drive in 2061, that's for sure. (What hard drive have you owned for even 10 years?)

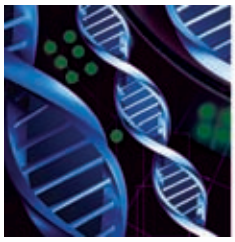
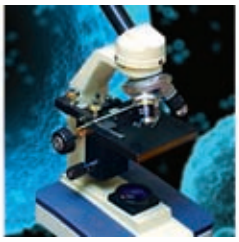
If, indeed, we care about sending our recordings into the next century, we'll have to tend them like a garden. Consumer magnetic tape begins to deteriorate after about 15 years, so the time to convert your old audio and video tapes to digital is right now. Giant hard drives are cheap these days, and Google has plenty of tutorials on how to rescue those memories.

The next step is to make a commitment: that you will revisit your recordings every 10 years. If your digital files are to reach your great-grandchildren, somebody, or generations of somebodies, will have to copy them from one hard drive to the next and from there onto solid-state drives, then to nanotubes, then to brain implants—whatever the latest storage medium happens to be. And it's not just the storage medium that will change; the file formats will have to be migrated, too. AVCHD probably won't be the state of the art in video recording in 2021, but there will certainly be software that can convert it to whatever is.

That way some of our photos, videos and documents will reach the audiences of 2161. Maybe only a tiny percentage—but enough to make your descendants grateful that you made that once-a-decade effort. SA

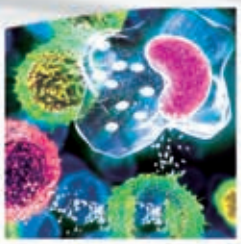
HOW TO DIGITIZE YOUR ANALOG MEMORIES
ScientificAmerican.com/apr2011/pogue

Illustration by James Yang



Malaysia Innovation: A Vision For 2020









MOSTI




INTRODUCTION BY THE HONORABLE DATO' SRI MOHD NAJIB BIN TUN RAZAK, THE PRIME MINISTER OF MALAYSIA

"It is heartening that the story of Malaysian innovation appears once again in *Scientific American*. Nearly 20 years have elapsed since "Malaysia 2020" was published in *Scientific American*. "Malaysia 2020" included an introduction by former Prime Minister Tun Dr. Mahathir bin Mohamad, who described Malaysia's vision and strategic plan to become a fully developed nation by the year 2020. Much has transpired since then, and Malaysia is well along the path to achieve this goal.

Several of the milestones along this path have been noted by external organizations, such as the World Economic Forum, which ranked Malaysia 21st in its Global Competitiveness Report. The report which highlighted Malaysia's flexible labor market, ranked Malaysia above two European nations - Spain and Luxembourg. In addition, a survey from IMD business school of Lausanne, Switzerland placed Malaysia in the top ten of the world's most competitive economies.

THE HONORABLE
DATO' SRI MOHD NAJIB BIN TUN RAZAK
PRIME MINISTER OF MALAYSIA

But we cannot rest where we are. To accelerate this economic development, Malaysia has ambitious plans to become a global leader in education and research as well as diverse industries such as biotechnology, pharmaceuticals, electronics, food, finance, environmental engineering, and clean energy.

To help drive these new, high-skilled, high-value sectors, I launched the Economic Transformation Program. The program had two key components. The first includes National Key Economic Areas which identify, prioritize and align support for priority sectors and major projects that will drive economic growth. The second component involves a set of Strategic Reform Initiatives, such as efforts to reenergize the private sector, to further develop the skills of our workforce, and to ensure sustainable growth.

It is within this dynamic framework that I welcome *Scientific American*'s focus on innovation and this opportunity to talk about Malaysia's journey. For innovation to flourish here, we must attract a large community of creative individuals from diverse fields and foster an environment which welcomes innovation, risk-taking and creativity.

To this end, last year I announced the formation of a new unit under my office, called the Special Innovation Unit (Unit Inovasi Khas or UNIK). It is working to involve and align stakeholders and elements in our innovation ecosystem, including our education system and universities, government programs, innovation funding and skill development programs. This Special Innovation Unit will drive strategies and policies, while a National Innovation Centre will serve as its implementation arm.

Today, innovation requirements, like economies, are more complex, dynamic and globalized than ever before. Funding of research institutes is no longer sufficient to achieve innovation goals. There must also be ways to capitalize and develop the fruits of this research. So the government is keen to extract the hidden wealth from decades of R&D work that has been conducted in Malaysia. We are working to commercialize our work and unleash the economic gains from this Intellectual Property.

To achieve this, the National Innovation Centre will actively search out promising research findings and seek to bring these ideas to market.

We look forward to future reports that assess the progress of these innovation-focused bodies and our drive to become a fully developed, high-income nation by 2020.

DATO' SRI MOHD NAJIB



Positioning science, technology and innovation to achieve VISION 2020

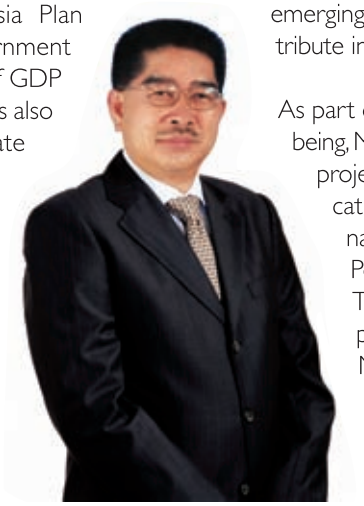
Malaysia has long recognized that investment in science, technology and innovation (STI) is essential in building a well-developed and prosperous nation. STI has indeed been fully embedded in Vision 2020, a national agenda which aims to propel Malaysia from the current middle-income status to that of a high-income, sustainable and developed nation. The government is taking proactive steps to create an ecosystem that spurs a culture of creativity and innovation.

To support the STI agenda, the government will continue to strengthen the existing institutional structure. This includes strengthening the office of Science Advisor to the Prime Minister, which is tasked to develop a framework for harnessing R&D, priority setting and provide a strong voice in the global arena. In addition, the National Science and Research Council has been established to provide the strategic direction in R&D.

Recognizing that innovation is vital in transforming the society, the government has recently set up the Malaysian Innovation Agency (MIA) to improve the innovation ecosystem. MIA will focus on commercializing IP's and it will work closely with MOSTI and other ministries. At the same time, MOSTI will under take initiatives to promote creative and innovative culture among the general public.

To attract, nurture and retain talents, the Talent Corporation has been formed. Additionally, the National Professors Council has been setup comprising 14 clusters with seven of them focusing on science, technology and engineering. Together, they would contribute towards reaching the target ratio of 50 research scientists and engineers (RSEs) per 10,000 in the workforce by 2015.

Under the Tenth Malaysia Plan (2011–2015), the government will allocate at least 1% of GDP on R&D. The government is also exploring ways to stimulate greater private sector investment on R&D.



DATUK SERI DR. MAXIMUS ONGKILI, MINISTER OF SCIENCE, TECHNOLOGY AND INNOVATION

In the area of biotechnology, the National Biotechnology Policy will enter its second phase this year with the theme - Science to Business. The policy focuses on industrial, agriculture and healthcare biotechnology and provides an integrated platform sustaining the industry's growth and progress. The biotechnology industry is expected to contribute about 5% to GDP by 2020, from 2.2% in 2009, and this reflects the huge investment opportunities in the Malaysian biotechnology sector.

As for the ICT sector, MSC Malaysia will enter Phase 3 this year: This will focus on infusion of ICT across all economic sectors to make Malaysia a vibrant hub for the creation of ICT solutions and to enhance national competiveness. The contribution of the ICT industry to GDP is targeted to increase to 10.2% by 2015, from 9.8% in 2009.

Further, the government will continue to focus on nanotechnology, oceanography and renewable energy. These sectors are vital as they are an integral part of the new and emerging resources of growth and contribute in achieving our vision.

As part of efforts towards societal well-being, MOSTI will continue with its CSR projects through Technology Application Programs. Based On the national philosophy of 1 Malaysia: People First Performance Now, TAPMOSTI@COMMUNITY projects, which aim to translate MOSTI-funded R&D outcomes to wealth, would be continued throughout the country, benefiting the target groups.

Efforts to transform Malaysia into a developed nation are led by the Prime Minister Dato' Sri Mohd Najib Tun Abdul Razak himself. Last year, he unveiled the New Economic Model premised on high income, inclusivity and sustainability to enable the benefits to be broadly shared across our multiracial and pluralistic society.

mosti.gov.my
ongkili.mosti.gov.my

Malaysia attracts thousands of youths from over 150 countries to pursue their higher education through comprehensive packages that combine tourism with education.

Malaysian innovation model will inspire change in the developing world

Innovation is an essential part of evolution. In every sphere of nature innovation fuels continuous change and adaption and ceases only when the state of perfection is achieved.

Mirroring this, every individual, every industry and every government on planet earth engage in acts to progress their current state of being so they may transform into better status (whatever that might be is a matter of opinion).

The world is at the crossroads of change - for better or worse

This pursuit has brought the world to a crossroad where collectively we either make a quantum leap for the better or plunge further down into greater destruction. We know now that change must be a conscious effort to create outcomes that are sustainable and conducive to a safer planet for all the peoples of the world.

The change that Malaysia is embarked on is exactly that, albeit on a smaller scale and benefitting less people than the entire global population.

For a nation that was condemned to fail in the first flush of independence back in 1957, we have made progress that is nothing short of remarkable.

Dismissed as a two-commodity economy because of our total dependence on tin and rubber back then, we have evolved because innovative decisions taken at the right time by our past leaders have kept up the momentum of growth and progress.

In the 1990s Malaysia was in the grip of Vision 2020, a blueprint to achieve fully-developed-nation status by the year 2020 as postulated by Malaysia's fourth Prime Minister Tun Dr Mahathir bin Mohamad. It was a ground-breaking vision that brought focus to the entire nation. It energized both the public and private sectors and it also inspired the developing world to emulate a similar roadmap for the future.

The coming years will see the country move into new directions because of bold decisions made by a government that continues its progressive journey based on consensus and democratic principles.

"Innovation is an important national agenda. The Government will transform Malaysia through a comprehensive innovation process, comprising innovation in public and private sector governance, societal innovation, urban innovation, rural innovation, corporate innovation, industrial innovation, education innovation, healthcare innovation, transport innovation, social safety net innovation and branding innovation."

YAB Dato' Sri Mohd. Najib Tun Abdul Razak
Prime Minister, Malaysia
23 October 2009

"The end result of innovation is a better and improved life for the citizens of Malaysia and this is my main drive in pushing innovation to the centre stage and making it a national agenda."

YAB Dato' Sri Mohd Najib Tun Abdul Razak
20 June 2010 Malaysia: Innovation Nation National Conference

Malaysia: a beacon of hope in a sea tossed by conflict and controversy

The government led by Dato' Sri Mohd Najib Tun Abdul Razak has stitched together a colourful quilt of social and economic programmes to achieve transformation of a scale never attempted before.

To move the nation from one category to another where all stakeholders are pitched into a battle with giants is indeed a daunting task. The nation is being primed now to strengthen muscles and gear up to take the game to a new level. The preparation is tough but it is something that must be done and as we have proven to the world before, we can do it.

Essentially what Dato' Sri Najib has achieved is balance. He has been courageous in his ideas, persuasive in his presentation and determined to be the voice of reason as he puts forward a new economic model to chart Malaysia's growth into the next era of higher value, higher productivity and higher income growth. The plan he has put forward is holistic, tackling all stakeholders to embrace creativity and innovation as vital elements for change to take place.

The Prime Minister, keenly aware of the global scenario took the first step in liberalizing the capital market to allow foreign investors to use Malaysia as a base for their regional and international operations. Growth, he said then, would be driven by investments in technology, talent, infrastructure, R&D and marketing to maximize long-term revenue growth and enhance market vibrancy.

Building the ecosystem for innovation

The Najib Government has been diligent in its planning knowing that innovation cannot take place in an isolated manner and that it must be pervasive, hence the step-by-step approach in introducing the New Economic Model, beginning the 1Malaysia drive, launching the Government Transformation Programme and the Economic Transformation Programme. The plans are ambitious and huge because the exercise of moving the economy into a higher category demands these changes.

An agent of change for the developing world

The policies devised and steps taken by this country in its journey over the last five decades have provided the bridge many developing nations have adopted to move their economies to new levels.

Malaysia is changing the education landscape of countries in southern Africa through Limkokwing University that attracts thousands to enroll into programmes customized to serve the interests of African youths.

This country has been a role model nation to the developing world and the new initiatives now undertaken are being studied with interest and anticipation. It won't be wrong to say that upon Malaysia's success rests the fate of other nations wanting to emulate and attain the same results.

This is no idle boast as Malaysia has been actively engaged with countries like Botswana, Lesotho, and Swaziland where you will find evidence of how Malaysian economic policies have inspired similar visions.

Here, too, you will find how the education landscape is being transformed through direct involvement and engagement.

Malaysia - a global player in innovating education

Limkokwing University of Creative Technology is a case in point. It is a brand recognized worldwide amongst youths who want a different approach to education, one that fits their aspirations and suits their lifestyle.

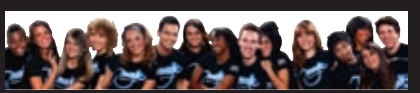
They are turning to alternative educational sources because they are not satisfied with the traditional approach. To illustrate this point it is worthwhile to note conclusions from a recent study on college education in the US captured in a book called *Academically Adrift: Limited Learning on College Campuses.* The study revealed that "after two years of college 45 percent of students learned little or nothing and after four years 36 per cent learned almost nothing".

To gauge the reality of this statement is to log in to the Limkokwing University's website where student enquiries from all over the world stream in non-stop 24 hours a day seven days a week. It is today one of the most popular university sites in the world with over 200 million hits from 222 countries/territories last year.

Globally this Made-In-Malaysia brand is making an impact through its controversial stand that education must change to be more relevant to today's environment and tomorrow's challenges.

LIMKOKWING

The university that changed the rules



Innovation happens when rules are broken. This is the story of a university that set out to put the student at the centre of empowerment, throwing conventions and traditions out the window. Its pioneering spirit in breaking new ground in higher education is awakening people to think differently about education and how it relates to a new generation growing up in a world dominated by technology.

Lawrence Watson

British academician Lawrence Watson found the Limkokwing journey a fascinating story of bold innovation that is transforming education.

"Limkokwing University will help us to create the knowledge and skill workers Lesotho needs. It is our hope to transform Lesotho by tapping into the creativity of our young people and build them into leaders who will be well-equipped to take Lesotho into a new future. Lesotho will not be the same again."

H.E. Pakalitha Bethuel Mosisili
Prime Minister of the Kingdom of Lesotho
15 October 2008

"Our people are so inspired it is impressive. Limkokwing University has become an international benchmark for innovation in higher education. With the establishment of a Gaborone campus, Limkokwing is an important player in our own efforts to build a more educated and informed nation."

H.E.Dr Festus G. Mogae
President of the Republic of Botswana
26 January 2008

"The Limkokwing University is globally identified by its unique philosophy of merging the best of East and West. This is something that young Cambodians will need as the country interacts with the global economy."

H.E. Samdech Akka Moha Sena Padei Teco Hun Sen
Prime Minister of the Kingdom of Cambodia
18 January 2008

"From Malaysia to Mayfair: the foreign university that is sending out shivers in the higher education world."

Headline carried by the Independent newspaper, UK when describing Limkokwing University's opening in London in October 2007

Tan Sri Dato' Sri Dr Limkokwing
President,
Limkokwing University of Creative Technology,
Malaysia Design Innovation Academy,
Branding Innovation Centre.
www.limkokwing.net



Interview with: Dato' Dr Kamal Jit Singh CEO UNIK

Kamal@pmo.gov.my

Q What does Malaysia have to offer with regards to innovation?

Lots. We are a melting-pot of various cultures, giving us the diversity that is crucial for innovation. Location wise, we are at the heart of ASEAN, a group of emerging nations that has a population base of about 500 million people. Malaysia has one of the oldest rainforests in the world, hence the opportunities that exist for furthering research in various disciplines is staggering. Just about every American and Japanese electronics company has manufacturing facilities in Malaysia; including significant R&D. We have a strong English-speaking talent pool, with good technical and managerial skills. Malaysia is a good story.

Q What are you seeking?

The possibility of partnering with international players, to take existing innovations to the market, to jointly undertake further work required to complete a particular product or to offer Malaysia as a test-bed to test innovative products and services. American companies and the scientific community should explore working with Malaysia. Sometimes, what doesn't work in the western world may be a perfect fit in Asia. Your "hidden wealth" could be realized outside your backyard and Malaysia could be the springboard for this to happen. Talk with us, let's see how we can help each other.

Q Which areas are of interest to you?

Malaysia has substantial strength in a number of sectors, so these are the ones we want to further build on. We are strong in plantations, manufacturing, oil and gas, the services sector and Islamic Finance. More than a decade ago, we started a major development called the "Multimedia Super Corridor" that is focused on ICT. We are already making inroads into bio-technology. These are some of the sectors where we can bring value to the table. Of course, we also want to venture into new areas such as clean or green energy, from both a technology as well as a services perspective.

DATO' DR KAMAL JIT SINGH

Q Are you relying on organic growth or is there another strategy?

Organic growth will not get us to our objective in time – Malaysia has laid out ambitious plans to become a developed nation by the year 2020. We have to ignite growth using various methods. One of them is by developing large areas where industry can develop and flourish. Innovation happens when folks from universities can intermingle with entrepreneurs and corporate honchos. Malaysia is providing several playgrounds for this to happen, in what we call "corridors". The Iskandar Corridor for example, is just minutes north of Singapore and has already attracted world-class universities to setup their campuses there. Both large and small enterprises dot this entire corridor, providing tremendous opportunities for organic and inorganic growth. The Iskandar Corridor is only one example – we have many others in the country, focused on individual niche areas. The Corridors are magnets that foreign companies should seriously investigate.

Q Innovation is a long-term game. Is Malaysia ready to play ball?

Yes, we are. Malaysia has always been an open nation and our interest to partner or collaborate is obvious from our track record. We understand that innovation does not take place in isolation and it is really the end-result of many parties working together to create cutting-edge products or technologies. Our government is serious enough that this special innovation unit is placed directly under our Prime Minister – it's his brainchild in the first place. The Prime Minister is breaking old molds and is innovating government itself. Malaysia's commitment to innovation has never been more serious.

UNIK
SPECIAL INNOVATION UNIT





Transforming higher education, Universiti Sains Malaysia

Established as the second university in the country in 1969, Universiti Sains Malaysia (USM) was first known as the University of Penang.

The university has been developing and expanding since its inception, which started with the enrollment of 57 science-based students. Now, USM offers courses at undergraduate and postgraduate levels to approximately 30,000 students. USM has become a well-known university locally and internationally.

The USM main campus is located in one of Malaysia's most beautiful spots, the tropical island of Penang (better known as the Pearl of the Orient), which now is connected to the mainland by a two kilometer causeway. Penang, known for its diversity, beauty, culture and food, is an ideal location for any student. The island has seen steady growth in the past decade and is also regional headquarters to multinationals such as AMD, Motorola and Intel.

There are two USM branch campuses, one at Kubang Kerian in Kelantan (approximately 300km from the main campus) known as Health Campus and the other at Nibong Tebal (approximately 50km from the main campus), known as Engineering Campus. The former houses the School of Medical Sciences, School of Health Sciences and School of Dental Sciences, while the latter houses the six Engineering Schools. Currently, the total enrollment is more than 8,000 post graduate students from 60 nations.

Collaborative research under one roof...

Is a difficult task for many institutions of higher learning but USM has created the Centre for Chemical Biology (CCB@USM), overcoming the challenges by understanding the value of collaboration from both a national and international perspective. More than 30 collaborative partners are located throughout Malaysia, Asia Pacific, South Africa and the United States.

One of the outstanding examples of these collaborative efforts is the decoding of the rubber tree genome, announced in October 2009.

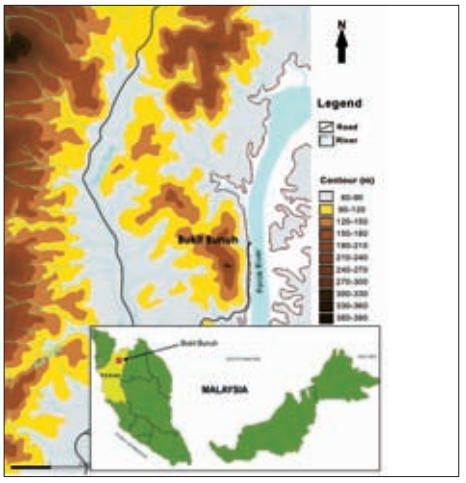
Rubber happens to be Malaysia's second most important cash crop contributing to a multi-billion dollar industry. It follows logically that Malaysia is motivated to keep its leadership position in the field and as a leader CCB@USM undertook the project bringing people and technologies together.

USM became the first university in the world to produce a draft of the 2 billion base genome of the rubber tree *Hevea brasiliensis*, underscoring Malaysia's potential of being the largest rubber producer in the world. Decoding the genome was done using its Seamless Genome-Based Discovery Platform, combining three Next Generation high-throughput sequencing platforms (454, Illumina/Solexa and SOLiD) along with the full transcriptome.

The breakthrough has led researchers to discover specific traits of the rubber tree that can be used for breeding and biotechnology applications, such as the improvement of rubber production, disease resistance, and high quality timber. With this knowledge, the development of improved rubber tree varieties will be greatly expedited as compared to the time it takes with traditional breeding techniques. USM researchers are also taking advantage of the discovery so that it can be applied to pharmaceutical and health applications.

Universiti Sains Malaysia, Penang Campus

Decoding Rubber Genome



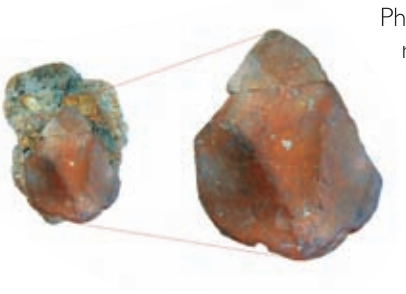
Bukit Bunuh Map

This project and its continuation into the functional genomics phase will train a young generation of scientists competent in genomics and bioinformatics, and lead to the development of a competitive platform for cutting-edge genome research in Malaysia. The positive financial implications of taking fundamental science to the field will mean substantially greater incomes for the small rubber holders who are often at the bottom end of the pyramid.

Bukit Bunuh and what it means for the world

The road to early human migration and development, once believed to have had its origins in Africa is now being challenged by a team of archaeologists from the Universiti Sains Malaysia. On a hill in Bukit Bunuh in the northern state of Perak (see inset map), stone tools dating back to over 1.83 million years were discovered, making them far older than the 1.5 million year hand axe which was found in Africa.

The extraordinary survival of the earliest archaeological evidence at Bukit Bunuh in the Lenggong Valley is due to the fact that a meteorite impact at 1.83 million years ago preserved many Palaeolithic stone tools in the melted suevite.



Hand Axes from Bukit Bunuh

The open-air site of Bukit Bunuh records the earliest hominid presence thus far known in Southeast Asia with the discovery of some of the oldest hand axes in the world embedded in suevite formed from a meteorite impact and dated by the fission-track technique to 1.83 million years ago. Given that the hand axes had to be present prior to the meteorite impact, human occupation of the site must have predated the impact. Therefore, this site would have been occupied by man much earlier than 1.83 million years ago. This is also one of the oldest dates for an early man presence outside Africa, and it bears considerable consequences for current theories on evolution and the timing of human dispersal from Africa to Asia and elsewhere.

Phase one, commencing in 2001, revealed a 40,000 year old stone tool workshop that produced pebble tools such as hand axes. The second phase led to the discovery of thousands upon thousands of tools embedded into the suevites. These suevites (or boulders) were found scattered around the site and are native to only a few areas in the world notably Canada, Germany, Mexico, Spain and Russia. The suevites found in Bukit Bunuh Perak have been dated to approximately 1.84 million years old, indicating that the area had been hit by meteorite. New minerals were found inside these suevites arousing interest from geologists around the world.

The discoveries at Bukit Bunuh have earth shattering implications for archeology and geology, and if this 1.83 million years old finding of the stone tools is verified a rewrite of world prehistory may be necessary.

Suevite from Bukit Bunuh

The Archaeology team under Professor Mokhtar has not rested on its laurels; research on more recent civilizations has also been undertaken....

Using a variety of techniques, such as land surveys, remote sensing and geo physics the team has been able to map out an area consisting of 97 sites in the Bujang Valley (Kedah) for excavation. Presently 10 sites have been excavated, eight of which are showing evidence of 1st century architecture and two actually indicate evidence of iron-smelting activities.

Through a process known as optically Stimulated Luminescence (OSL), conducted separately at the University of Washington, Hiruzen Japan scientific lab and Korea's Conservation Science Lab, Mokhtar's team were able to identify the age of the artifacts to about 100AD.

In 2009, the Malaysian Government gave the green light for the team to undergo more study and excavation. Subsequent findings are of great significance to the history of the area as they point to commercial smelting activities being carried out there. Earlier studies and findings were based on religion with discoveries of ancient tomb temples.

Last year, his team discovered a 1,900 year old monument resembling a sun dial, constructed with detailed geometrical precision. It is thought to be the oldest man made structure in the region. When viewed from a regional perspective, and based on chronometric dating, this monument predates other man made structures in the area, notably Angkor Wat in Cambodia (1200AD) and Borobudur in Indonesia (900AD), a discovery that yet again may lead to a re-write of the regions history.

Mokhtar is now focusing his efforts on seeking evidence of humans in the area to further substantiate the team's findings.

Palm Oil and Vitamin E extensively researched at USM

It is a little known fact, but Malaysia is the world's main producer and exporter of tocotrienols, a potent form of vitamin E found abundantly in palm oil. Vitamin E consists of 8 molecules - 4 known as tocopherols and 4 tocotrienols. Most vitamin E preparations in the market contain only one form, namely alpha-tocopherol which is found in most edible oils like soybean oil. Tocotrienols are less known because they are not found in most edible oils such as those from sunflower, olive and soybean.

Recent studies have shown that, apart from their normal vitamin E activities, the tocotrienols possess unique biological activities not found with the tocopherols.

More importantly, Malaysia is also making medical progress in using the tocotrienol extracts from palm oil to lower risks of stroke and heart attacks and eventually, treat these degenerative diseases.

Leading this global race in finding natural sources to stem and treat these major killer diseases are Ipoh-based Hovid Group, Universiti Sains Malaysia (USM) and the Malaysian Palm Oil Board (MPOB). Heading the team is USM Professor Yuen Kah Hay.

Professor Yuen Kah Hay cited studies by Ohio State University that proved tocotrienols (but not tocopherols) can prevent programmed death of brain cells under stress by suppressing key cell signals.

Subsequent experiments on genetically modified mice which are prone to stroke also showed the tocotrienols could minimize damage to the brain cells.

In view of the promising neuro-and-vascular-protective effects, the present study in Malaysia is conducted on volunteers with MRI confirming white matter lesions (WML), or oxygen-starved brain cells which lead to bundles of neurons dying. The volunteers are randomized to receive the tocotrienol capsules or placebo over 2 years in a double blind manner (both researchers and volunteers do not know if they are taking placebos or the tocotrienols). An MRI of the brain is repeated on the volunteers after one year and again at the end of the 2 years. Changes in the volume of the lesions between the 2 groups will then be compared. The study is scheduled to be completed by the middle of this year.

"From the brain scans, we can tell if there is WML, a form of sub clinical brain infarct. This means the volunteer's brain vascular network is already unhealthy and at high risk of contracting stroke. If the results of our study show that the tocotrienols are neuro-protective, they can then be taken daily to prevent or minimize damage to the brain cells during a stroke episode," Yuen concluded. He also pointed out that the tocotrienols will be useful to other diseases such as diabetes, which lead to degeneration or damage of our central or peripheral nerves.

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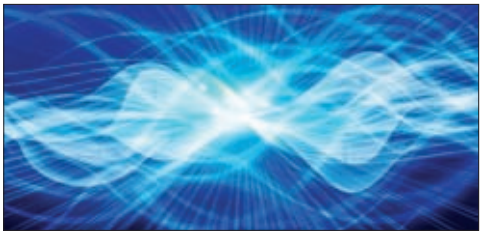

ASM's role towards innovating Malaysia

Science, Technology and Innovation (STI) offer Malaysia the greatest opportunity to turn ideas and creativity into a highly competitive business. At this critical phase of Malaysia's economic development, as is outlined by the trios of the New Economic Model (NEM) with its inclusiveness and sustainability, the Government Transformation Program (GTP) of putting governance as an enabler, facilitator and supporter of economic growth and finally the Economic Transformation Program, (ETP) which provides the road-map towards becoming a high income nation, ASM's role is to champion scientific discovery and use the benefits of science, engineering and technology to transform Malaysia into a high income nation. This is an ongoing challenge. As a leading agency, ASM has always prided itself in constantly harnessing science, technology and innovation with the clear objective of promoting economic growth through increases in productivity and competitiveness in the production of goods and services, all within the realm of sustainable development.

Innovation is the key to globalization and competitiveness as well as, being the heartbeat of development. In response to the call for innovation, ASM, on its part has undertaken numerous scientific programs to strengthen research and technological capacity. This is being done by placing the emphasis on fundamental research as well as the commercialization of research outputs, strengthening the institutional framework and management of science, technology and innovation in the country. These programs will lay the foundation and raise innovation up to a more competitive level, in line with the government's high income advanced economy drive for Malaysia.

TAN SRI DR. AHMAD TAJUDDIN ALI
PRESIDENT OF THE ACADEMY OF SCIENCES MALAYSIA

Foremost amongst the innovative programs undertaken by ASM is the Mega Science Framework Study on the five core areas, whose importance to humanity is highlighted by the U.N. Millennium Goals namely, water, energy, health and medicine, agriculture and biodiversity. The study undertook to develop a roadmap in fostering, promoting and managing the development and application of scientific knowledge and technological innovation for wealth creation, societal well-being and sustainability. This called for the pervasive, intensive and extensive use of science to identify and develop competitive knowledge and STI opportunities for commercialization in various sectors of the economy. The study also identified priority sectors where Malaysia possesses a comparative advantage. It identified the knowledge gaps and proposed solutions, targeted *niche* areas for commercial exploitation, and finally ensured that advances in science would be used for the benefits of society. As such, the outcome of the Mega Science Study will not only reaffirm the potential of science, technology and innovation in wealth creation, but will also serve to impress that STI needs to be driven by cutting edge technologies, underpinned by a strong R&D and innovative base.

Other areas that encourage the development of science and innovation include outreach programs through inculcating the development of young scientists and the Brain Gain Program which encourages the return of overseas Malaysian experts to impart their skills and knowledge in efforts to build up local expertise. The publication of *Estidotmy*, a popular monthly science magazine, also serves to generate interest in science, education among primary and secondary school students. Other ASM publications include monographs on various scientific topics, lectures of Nobel Laureates and eminent scientists, and biographies of prominent Malaysian scientists.

ASM's efforts in promoting creativity and innovation would not have been successful, had it not been for the strong support and a partnership among all its stakeholders, especially the Ministry of Science, Technology and Innovation Malaysia, as well as industry, universities and research institutions. Guided by the New Economic Model, the Government Transformation Program and the Economic Transformation Program, ASM will continue to be the driving force and contribute to promote and inculcate creativity and innovation among Malaysians.

About the Academy

The Academy of Sciences Malaysia as a learned body of Science, Technology and Innovation (STI), performs an unparalleled public service by bringing together experts in all areas of scientific and technological endeavor to address critical national issues relating to science, engineering and technology and provide strategic input to the government and the public.

The Academy also extends its expertise and advisory services to various STI stakeholders ranging from government, ministries and agencies, institutions of higher learning, research institutes, industry as well as international STI organizations.

The Academy of Sciences Malaysia was established under the *Academy of Sciences Malaysia Act 1994* which came into force on 1 February 1995. It was officially inaugurated by the former Prime Minister, YABhg Tun Dr Mahathir Mohamad on 8 September 1995.

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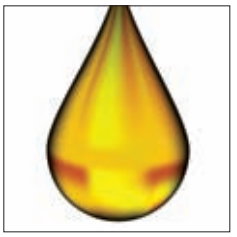


Oil palm, the crop of the future

"The Ministry of Plantation Industries and Commodities, through the Malaysian Palm Oil Council has set up a dedicated fund known as the Malaysian Palm Oil Wildlife Conservation Fund (MPOWCF). The fund was launched in 2006 and bears testimony to the commitment from both the Malaysian Government and the Malaysian palm oil industry in sponsoring studies and programs that will help the industry in the conservation of the environment and its biodiversity" extract from an interview with Minister Bernard Dompok.

Tan Sri Bernard Dompok, is effectively one of Malaysia's most strategic ministers leading the charge for Plantation Industries and Commodities. Two of Malaysia's largest cash crops come under him; rubber and oil palm *(elaeis guineensis)*.

The facts on oil palm are often misinterpreted in the West under mistaken and sometimes incorrect assumptions. The uphill battle to correct some of the misperceptions has been a long one but with efforts from The Ministry and bodies like Malaysian Palm Oil Council, inroads have been made in a slow but very effective manner.

According to Minister Dompok, the campaign by Western NGO's against palm oil has been misleading and disingenuous. When related to deforestation it is simply misinformed.

Dompok states that Malaysia retains 56 percent of its land under permanent forest and has cultivated all land reserved for agriculture. This means that no land is converted from primary forest to oil palm plantations. Instead palm oil is the driver for economic growth and the need to reduce poverty leads to agricultural development. The key point here is that a reduction in the use of palm oil will not lower the rate of land clearing in developing nations. Indeed given that oil palm has one of the highest yields and highest income returns per hectare of any crop, a shift away from oil palm will lead to the clearing of more land to make up for that lost income.

Palm oil and food security

On the issue of food security and how palm oil contributes positively, the Malaysian Palm Oil Council, under the steady guidance of its CEO, Tan Sri Dr. Yusof Basiron, has been very active in explaining and demystifying the misconceptions.

TAN SRI DR. YUSOF BASIRON
CEO MPOC

At the Oil Technologist Association of India conference last year which focused on food security, green energy and the environment in New Delhi, India, Dr Basiron addressed the issue of food security from a very pragmatic perspective.

Initially explaining how the worlds' population is in a steady upward growth curve and is expected to reach 8 billion by 2030, Dr. Basiron inferred that there will be many more mouths to feed and that ever since the beginning of time, the requirement to satisfy hunger has always been a basic need of mankind. Consequently, as population increases, food supply must increase in tandem.

Illustrating that the oil palm is an important agricultural crop which yields three important sources of food, namely palm oil, palm kernel oil and palm kernel cake. An average of 3.7 tons of palm oil, 0.4 tons palm kernel oil and 0.5 tons of palm kernel cake is obtainable from one hectare of land. While the first two products can be used for human consumption, such as cooking oil, margarines, etc. Palm kernel cake is used as animal feed.

Dr. Basiron also noted that Malaysia and Indonesia are the two largest palm oil producers in the world. Together they constitute 85.3% of the world's production.

According to Dr. Basiron, one of the most important hurdles to overcome, during the pursuit to achieve food security is the diminishing availability of already scarce arable land. Due to palm oil's high productivity, whereby it can produce 4.13 tons per hectare versus 0.75 (rapeseed), 0.58 (sunflower) and 0.40 (soybean), 11 times less land is needed to obtain the same amount of vegetable oil if oil palm substitutes soybean completely. The extra land saved, could then be used to plant other crops.

Dr. Basiron concludes that oil palm is the leader that has the greatest potential to overcome food insecurity and is capable of doing it in a very sustainable way since it requires the least amount of land to produce the same amount of oil.

MPOC

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Malaysian rubber industry leads the way to environmental conservation and sustainability

Malaysia is one of the world's major producers of natural rubber and has been actively involved in research and development with regard to production of this important commodity. The Malaysian Rubber Board, the custodian of the rubber industry in Malaysia, has two research centers, Rubber Research Institute of Malaysia (RRIM) in Malaysia and Tun Abdul Razak Research Centre (TARRC) in the UK. Established in 1925 and 1938 respectively, both institutes have made significant contributions to the science and technology of natural rubber.

The current R&D activities carried out by the Malaysian Rubber Board (MRB) are to position the Malaysian rubber industry as a leader in technology, environmental conservation and sustainability. Innovations by MRB are all-encompassing and contribute to the overall spectrum of the natural rubber industry. The two latest areas to be highlighted are specifically natural rubbers and rubber biotechnology.

Specialty Natural Rubbers for Advanced Applications – *From Nature for Nature*

Ekoprena™ and Pureprena™ are two forms of specialty natural rubbers developed from renewable resources. In addition to having advanced properties desirable for most of applications for rubber products, these specialty rubbers respond to the demands of the latest global trends toward environmentally-friendly or green rubber products and sustainable development. This is achieved through the efficient use of natural resources and energy to improve the carbon life cycle of rubber products.

Some products made from Pureprena™

Ekoprena™ is a form of epoxidised natural rubber obtained by epoxidation of natural rubber latex. Ekoprena™ is established as a green material for rubber products as it is produced from a renewable natural source, unlike synthetic rubbers which are derived from non-replenishable petroleum. Currently two grades of Ekoprena™ are produced commercially; Ekoprena 25™ and Ekoprena 50™, containing 25 and 50 more % epoxidation contents, respectively.

Epoxidation essentially improves wet grip characteristics of natural rubber. In particular, its oil resistance and gas permeability are equivalent to those of specialty synthetic rubbers. Ekoprena 25™ offers the best balance of wet grip and rolling resistance for tire applications. Currently there is a major demand of Ekoprena™ as it contains 'green' material with advantageous properties which can replace synthetic rubbers in the manufacturing of environmentally-friendly or 'green' tires. Thus, with the increasing demand to reduce fuel consumption, Ekoprena™ will play a significant role as a green material in the future development of tires.

Pureprena™ is an eco-efficient form of deproteinized natural rubber with specific raw rubber properties. This specialty rubber is very low in nitrogen, ash and volatile matter contents as well as being light in color.

Pureprena™ is produced by treating fresh natural latex through biochemical hydrolysis which denatures all naturally-occurring proteins in the latex. The removal of these non-rubber components adds special attributes to the rubber which enhances its suitability for specialized rubber product applications.

Pureprena™ as a specialty purified natural rubber, whether in dry rubber or latex form, has generated a lot of interest in the rubber product manufacturing industry. The importance of Pureprena™ is in its dynamic engineering applications when compounded using the soluble efficient vulcanization system. Pureprena™ shows low creep and stress relaxation, low water absorption, low compression set and a more consistent modulus when subjected to conditions of variable humidity. Pureprena™ is therefore suitable for a niche market where the requirements for such properties are very stringent, not only for the rubber industry,

LEMBAGA GETAH MALAYSIA
LGM
MALAYSIAN RUBBER BOARD




but also in medical, pharmaceutical and food industry applications.

Currently the technologies for Ekoprena™ and Pureprena™ are being transferred to Felda Rubber Industries Sdn. Bhd. and Mardec Processing Sdn. Bhd., two well established and major rubber processing companies, which will ensure commercial availability and uptake by rubber manufacturers worldwide beginning in 2012.

Sequencing the Natural Rubber Genome

Traditional rubber tree improvement, as with any wood species, is a lengthy and difficult process. The knowledge accumulated by generations of rubber researchers and growers, in tandem with modern technological advances is, about to change the situation. In October 2010 the Malaysian Rubber Board reported the completion of a high-quality draft genome sequence of one of the most promising commercial clones of *Hevea brasiliensis*, RRIM928. Sequencing was carried out by TARRC in collaboration with the UK's Genome Analysis Centre (TGAC), and was completed within nine months. In parallel, high coverage transcriptome data of leaf and latex in the form of Paired-End RNA 2X100 nt reads (Illumina™) were generated at RRIM.

With an estimated two billion bases, the Hevea genome is one of the largest plant genome sequenced to date; it is at least four times larger than the genomes of cacao and rice, and seventeen times larger than the genome of the model plant Arabidopsis thaliana. The considerable challenge posed by both the size and anticipated complexity of the Hevea genome, was overcome by the TGAC team, using two complementary 'Next Generation' sequencing platforms, to generate the draft sequence. Combining the massive throughput of the Illumina™ platform, with the longer read length of the Roche 454 platform, enabled fast and accurate assembly and produced approximately 80-fold sequence coverage of the genome.

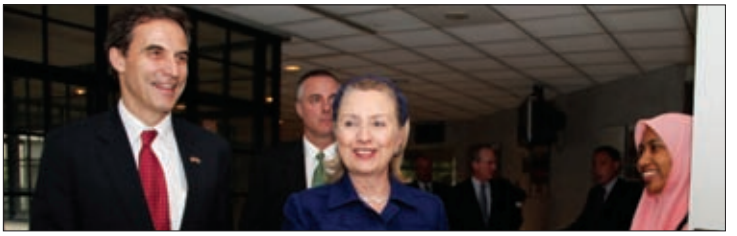
DATUK DR. SALMIAH AHMAD
DIRECTOR GENERAL OF THE MRB

Together, genomic and transcriptomic data, along with an existing collection of 35,000 latex Expressed Sequence Tags (ESTs) generated by the RRIM, were used for genome annotation and assembly. In order to close gaps between assembled scaffolds, traditional Sanger end-sequencing of an RRIM928 fosmid library from leaf tissue is being used. Bioinformatic analysis of the combined data estimates that the Hevea genome may contain in the region of 43,000 gene models, around 20% of which are functional genes.

The availability of the annotated Hevea genome sequence will now enable the development of a large database of molecular markers for the identification of genes involved in commercially important traits and thus help improve the efficiency of current breeding schemes. Shorter maturing time, higher latex yield, better timber and rubber quality, production of pharmaceutical chemicals, superior disease resistance and tolerance to climatic changes are all targeted to help make natural rubber the leading 'green' commodity in the world.

The Malaysian Rubber Board aspires to be a global center of excellence for rubber. The main research activities focus on sustaining the industry in Malaysia through production of value added or niche products 'engineered for performance'. Due to the recent surge in demand and the increase in the price of natural rubber, the Government of Malaysia has decided to give rubber a special status and has now placed it together with twelve priority areas under the strategic banner of National Key Economic Activities (NKEA).

www.lgm.gov.my

United States Ambassador discusses US-Malaysia cooperation

I'd like to thank *Scientific American* (SA) for its foresight in developing this timely special supplement on Malaysia. And who better than SA to look at science, technology and innovation in this dynamic American partner. I was delighted to discover SA as a young student,and I know it continues to be an outstanding exemplar of American journalism, a publication that millions of readers around the world know and trust.

The United States and Malaysia have vibrant and extensive interaction on science, technology, engineering and innovation. To take this cooperation to an even higher level, U.S. Secretary of State Hillary Rodham Clinton and Malaysian Minister of Foreign Affairs Datuk Sri Anifah bin Aman on November 2, 2010 signed a bilateral Memorandum of Understanding (MOU) on Science and Technology Cooperation. The MOU provides a framework to facilitate even deeper collaboration, including stronger relations between our universities, their faculties, students and research networks. Through such capacity-building we can foster more innovation that is critical to energize knowledge-based economic growth in both our countries. More collaboration in S&T and knowledge-sharing can help provide solutions to shared global challenges, such as enhancing global health, improving food security, protecting biodiversity, developing clean energy, and strengthening critical infrastructure.

U.S. economic engagement with Malaysia is broad and deep. The United States is the largest foreign investor in Malaysia, with extensive investments in the electronics, oil and gas, and solar industries. Investment by U.S. electronics and other technology companies has played a major role in Malaysia's development, including as a major producer of electronics. Many of these companies engage in extensive research and development work in Malaysia, employing some of Malaysia's best and brightest engineers. Less known is the important role of U.S. energy companies in providing advanced know-how in the offshore oil and gas sector, in partnership with Malaysia's national oil company, Petronas.

Tens of thousands of Malaysians have degrees from U.S. universities, and thousands more are studying in the United States today. And U.S. scientists and engineers have collaborated with their Malaysian counterparts to discover unknown species, develop new medicines, enhance agricultural productivity, and better understand emerging infectious diseases and the threat of pandemic influenza.

AMBASSADOR PAUL W. JONES

The Malaysian government seeks to increase support for S&T innovation as a growth engine, symbolized by the signing of the bilateral S&T MOU, increased private sector collaboration, and develop a stronger basic research profile, exemplified by Prime Minister Najib's intent to form an international science advisory council with the New York Academy of Sciences.

We will be working further to strengthen these ties. We want to cultivate further people-to-people and researcher-to-researcher collaboration. And we want to exchange views on creating enabling policy environments for innovation, including state-of-the-art intellectual property protection and policies for biotechnology and nanotechnology. We will also be exploring opportunities for further collaboration through the new program of science envoys. This program, announced by President Obama in Cairo in June 2009, is a centerpiece initiative to implement U.S. global engagement in science and technology. These preeminent scientists will seek to deepen existing ties and foster new relationships with foreign counterparts and gain insights from other nations about potential areas for new or greater collaboration.

At the same time, we also recognize the potential for some technologies to be misused. In this regard, we welcome the actions Malaysia has taken and is taking to establish and enforce effective measures to prevent the proliferation of nuclear, chemical, or biological weapons and their means of delivery. We will continue to work with Malaysia to achieve our common objectives in this critical area.

The future for bilateral U.S.-Malaysia S&T collaboration is bright. Together, it can help us better meet shared global challenges and build a prosperous and secure global future. I thank *Scientific American* for its efforts to support those goals.




Sabah-Borneo, nature's gem

"Malaysia Truly Asia" is the tried and tested advertising slogan which has considerably helped brand Malaysia and implant its unique identity to the world. The country is truly Asian and is made up of a potpourri of ethnic races, cultures and religions. It is precisely this ethnic mix or cultural cappuccino that brings out the best in Malaysia. From its food to its traditions the country is one of the most diverse and yet tolerant nations in Asia, if not the world. It is home to three main races, Malay, Indian and Chinese all practicing their respective religions alongside a multitude of many Christian Churches which prevail throughout the country.

A focus on Sabah is rich in diversity of landscapes and people as well as plant and animal life. Its landscapes range from long white sandy beaches to magnificent rainforests and Malaysia's largest freshwater floodplain, home to Borneo's unique proboscis monkey and the orangutan. Dominating the scenery is South East Asia's largest mountain Mount Kinabalu, towering at an impressive 4,095 meters. It is the focal point of Kinabalu Park, Malaysia's first World Heritage Site (Unesco November 2000). Sabah is also the perfect place for adventure sports and offers world scuba diving sites; Palau Sipadan and Layang-Layang. Hiking, white water rafting and a range of sea sports as well as horse riding and golfing are readily available.

Biodiversity and Conservation

The tropical rainforests are the world's most diverse forests and Borneo is home to one of the greatest collections of plant diversity on earth. Sabah's forests house more than 3000 tree species. No other rainforests in the world show such abundance and diversity of a single family of big trees. Borneo has a very rich and diverse palm flora with about 280 recorded species representing more than 10% of the world total.

No less impressive are available estimates for Borneo's fauna. The rich bird fauna has an amazing diversity of around 622 species, of which 434 are known to have been breeding. The Bornean snake fauna includes at least 154 species. Insects are by far the most numerous and at least 5000 beetle species alone have been recorded in Gunung National Park. Other groups of mammal species to be sighted are Sumatran rhinoceros, proboscis monkey, red banded leaf monkey, silver leaf monkey as well as the group consisting of dolphins and porpoises.

Mount Kinabalu

Shangri-La Hotels commitment to the environment.

One of the best and most luxurious hotels in Sabah is Shangri-la's Rasa Ria located 45 minutes north of the capital city, Kota Kinabalu.

The hotel has its own nature reserve offering a first-hand glimpse into the Borneo jungle. It is the cornerstone of commitment and contribution towards responsible and sustainable environmental tourism, Encompassing 64 acres within the resort, the Nature Reserve is a conservation effort between the Sabah State Wildlife Department and Shangri-La Hotels and Resorts.

The Nature Reserve

The Reserve is aimed primarily at nature conservation and orangutan rehabilitation, with research, study and education activities carried out as well. The rehabilitation program for orangutans is the only one of its kind on the west coast of Sabah (Sepilok Rehabilitation Center in Sandakan on the east coast is the main orangutan rehabilitation center in Malaysia).

Among the activities available within the Reserve are the *nature walks, nocturnal animal watch, bird watching, mini canopy walks* and *in search of orangutans.*

Twice daily a ranger escorts groups through the reserve to view the orangutans in the wild, lured to proximity through a natural feeding program.

During a recent interview with the Minister of Tourism Dato' Sri Dr. Ng Yen Yen, it became very apparent that one of her objectives was aimed at changing the mindset, habits and attitude of Malaysians towards cleanliness. "It is important to promote cleanliness nationwide and to raise awareness to Malaysians on the importance of a healthy environment and be the champions responsible towards keeping their surroundings clean," she emphasized. "This has to come from the home and the heart," according to Yen Yen, "as well through education in the schools starting at a very young age."

DATO' SRI DR NG YEN YEN
MALAYSIA'S TOURISM MINISTER

Going one step further to consolidating the concept a new slogan, One Malaysia Green Malaysia was coined as well as a website outlining her vision for the country. The Minister of Tourism Malaysia, Dato' Sri Dr. Ng Yen Yen said. "To achieve this objective, the Ministry is taking the lead by establishing and promoting cleanliness as a standard for Malaysia as our country strives to maintain its position in the top 10 list of the most visited countries in the world."

SCIENTIFIC AMERICAN Travel

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Set a course for intellectual adventure on the Black Sea with your curiosity as a guide and Scientific American to take care of the details. Join Scientific American on the Bright Horizons cruise conference on Holland America Line's ms Rotterdam, sailing Rome to Athens October 1–13, 2011.

As you ply the wine-dark seas, join Dr. John Steele in tracing the astronomical legacies of the Babylonians and Greeks. Dr. Michael Wysession conveys the impact of volcanoes and tsunamis in the flow of civilization. Sit with Dr. Michael Benton as he brings dinosaurs to life. Tune in to Dr. Mohamed Noor, as he details the nature of species. Get the latest concepts on comets with Dr. Mark Bailey. Illuminate dark matter with Dr. Lawrence Krauss.

The Draconid meteor shower will punctuate your Black Sea sojourn. Typically a minor celestial event, the 2011 shower is forecast to be a humdinger.

Cover new terrain, from Rome to Odessa to the Kuiper Belt. Celebrate ancient civilizations and the current moment with a friend. **Find the how-tos and details at www.InSightCruises.com/SciAm-10** and join kindred spirits on a voyage of discovery.

Cruise prices vary from $1,799 for an Interior Stateroom to $5,299 for a Deluxe Suite, per person. For those attending our program, there is a $1,475 fee. Government taxes, port fees, and InSight Cruises' service charge are $208.91 per person. **For more info please call 650-787-5665 or email us at Concierge@InSightCruises.com**

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COSMOLOGY

Speaker: Lawrence Krauss, Ph.D.

Quantum Man: Richard Feynman's Life in Science — It took a man who was willing to break all the rules to tame a theory that breaks all the rules. Learn about the scientific legacy of one of the greatest and most colorful scientists of the 20th century, and in turn get insights into the questions driving the science of the 21st century.

An Atom from Greece — Every atom in your body was once inside a star that exploded. Lawrence Krauss will present the life history of an atom in a glass of wine you will have with dinner, from the beginning of the universe to the end. The story is rich in drama and surprises, and will leave you thinking differently about your place in the cosmos.

The Dark Side of the Universe: From Black Holes, to Dark Matter, and Dark Energy — The most interesting things in the universe apparently cannot be seen. Learn why scientists are fascinated by them, and why they hold the key to understanding our origins, and our future.

Hiding in the Mirror: Extra Dimensions, CERN, and the Universe — The largest machine humans have ever built has turned on in Geneva, and happily has not created a black hole that destroyed the world. But what might be discovered there, and will it tell us that there is, literally, infinitely more to the universe than meets the eye?

PALEONTOLOGY

Speaker: Michael J. Benton, Ph.D.

The Life and Times of the Dinosaurs — Many people think images of dinosaurs in museums and films are largely imaginary. Find out how paleobiologists reconstruct the life of the past using a combination of three modern scientific methods. Dr. Benton will share the standard tools, unexpected finds, and new engineering approach to understanding how these ancient giants looked, moved, and fed, putting dinosaur discoveries and imagery in a new light.

Origins and Extinctions — Life has existed on Earth for four billion years, punctuated by origins and extinctions. From the origin of life to the origin of humans we'll look at one of the grandest questions in science: where did we come from … and can we be sure? Dr. Benton then explores international research from North America, Russia, China, and Europe on the causes and consequences of extinctions.

Origins of Modern Biodiversity — Life today is hugely diverse. Darwin wondered at this richness, and argued that life was more diverse than it had to be! Research efforts now concentrate on reconstructing the evolutionary 'tree of life' using genomes and fossils, bound by massive computing power. Get the scoop on biodiversity and the latest on biogeographic investigations, fossil data, and number crunching of the new genomic sequences.

The Dinosaurs of Eastern Europe and the Mediterranean — In the days of the dinosaurs, continental drift and sea level change led to ever-changing geography. See how geologists create paleogeographic maps to locate the dinosaur fauna of what is now Eastern Europe. Meet colorful characters from early days of paleontology. Learn how regional research changed during the Iron Curtain days and how current researchers are bringing Europe's unique dinosaurs back to life.

COMETS

Speaker: Mark Bailey, Ph.D.

Meteors, Meteor Showers, and the Draconids — Meteors or shooting stars are fragments of dust from comets, burning up in the Earth's atmosphere. The time of this lecture coincides with a predicted outburst of the annual Draconid meteor shower. It is expected that activity will increase to a peak over a 2- to 3-hour period beginning around 8pm, with up to several hundred meteors per hour possibly being seen, depending on local weather conditions. After a brief introduction to meteors and meteor storms, we go up on deck to observe the "dragon's" fiery flame.

Comets and Concepts in History — Humans have a love-hate relationship with comets. We'll look at the oldest theories of the nature of comets and the role they played in astronomy's development. Blaze a trail with Dr. Bailey through the historic observations, arguments, and theories leading to the realization that comets are largely Oort cloud products, formed with the Sun and planets 4.5 billion years ago.

The Life, Times, and Persistent Puzzles of Comets — Broaden your horizons delving into 20 years' worth of discoveries on comets and their origins — whether in the Edgeworth-Kuiper belt just beyond Neptune, the trans-Neptunian disc, or the Oort cloud. Survey the natural history of comets in the inner solar system, and discover the persistent puzzles and uncertainties in this vibrant, active field of solar-system research.

Risks Posed by Comets and Asteroids — Comets occasionally descend on the Earth with catastrophic effect. At one extreme, such impacts can change the course of evolution disrupting the normal "Darwinian" process. At another extreme, relatively small impacts may have important implications for the development of civilization. Find out how the risk of rare, high-consequence events is assessed.

ANCIENT ASTRONOMY

Speaker: John Steele, Ph.D.

Astronomy in Ancient Babylon — Cuneiform writing on thousands of clay tablets documents the astronomical activity of the ancient Babylonians. These texts circa the first millennium BC, include lists of astrological omens, astronomical observations, and calculations of the positions and phenomena of the moon and the planets. Join Dr. Steele

to investigate the astronomical traditions of the ancient Babylonians and their invention of scientific astronomy.

Ancient Greek Astronomy — How could Ptolemy insist that the earth was the center of the Universe? The ancient Greeks didn't invent astronomy, but they were the first to combine philosophy with mathematics to model the motion of the heavens using geometry. Along the way they figured out the size of the Earth, the distance of the moon from the Earth, and developed geometrical methods for modeling planetary motion. Delve into the legacy of Greek astronomy, and trace its impact in the medieval Islamic world and Renaissance Europe.

The Antikythera Mechanism: An Ancient Mechanical Universe — In 1900 sponge divers off the tiny island of Antikythera discovered an ancient Roman shipwreck laden with works of art. Almost unnoticed were the poorly preserved remains of a small mechanical device — the Antikythera Mechanism. Through painstaking reconstruction and analysis over the past century, we now know the device was a mechanical astronomical computer of great ingenuity. Learn the story of research on the mechanism — and what it has revealed about ancient Greek science and technology.

Eclipses in History — Eclipses are one of the most awe-inspiring astronomical events. Throughout history eclipses were viewed with fear, excitement, astonishment, and scientific curiosity. Take a look at how eclipses have been observed, interpreted, and commemorated in different cultures around the world and discover how scientists today benefit from ancient eclipse records.

EVOLUTION

Speaker: Mohamed Noor, Ph.D.

What is "Evolution" Anyway and Why Should I Care? — The mere word "evolution" conjures images in the public ranging from movie dinosaurs to something vaguely half-human-half-gorilla. What does the word evolution actually mean in the biological sciences, what is the evidence that it is true, and why should the general public know and care? In fact, evolution affects your everyday life, from your health to your livelihood — come learn why!

On the Origin of Species, Really — Although Darwin's book title suggested that he defined the origin of species, in fact, he only focused on the process of divergence within species and assumed the same processes "eventually" led to something that could be called a new species. Dr. Noor will talk about how species are identified (in practice and in principle), how to modern evolutionary biologists use this type of information to get a handle on how species are formed, and what questions remain.

Genetics, Genomics, and You: Don't Fear Your Genotype! — The missing element to Darwin's theory was how it worked in terms of inheritance. Genetics answered that. Today "personal genomics" issues span medical, legal, ethical, and other areas and pose big question. Get ready for discussion and a lab exercise to help understand the lingo, opportunities, and issues associated with living in the genomics era.

Life in the US Academic Sciences — What happens behind closed doors in the "Ivory Tower" of an academic scientist? Scientists at universities juggle multiple roles. What do these people actually do all day? What are these scientists trained well to do and what are areas where they really are not trained well? What is a typical career trajectory in the sciences, and how are scientists evaluated? Get an inside look from a noted academic.

GEOLOGY

Speaker: Michael Wysession, Ph.D.

Changing Climates, the Black Sea Flood, and the Rise of Civilization — The philosopher Will Durant said, "Civilization exists by geologic consent, subject to change without notice." The history of climate change illustrates this richly. Dr. Wysession lays out the factors controling the climate and how climate change has been the driving factor for the course of human history. You'll get a detailed look at the Black Sea Flood of 7500 years ago, and enrich your understanding of the impact of climate change.

Santorini and the History of Megatsunamis — 3600 years ago, Thera/Santorini saw one of most powerful volcanic eruptions known, leaving just the island ring we see today, burying the Minoan city of Akrotiri under 60 feet of ash, creating a megatsunami that devastated the entire Mediterranean. The the U.S. Northwest's 1700 M-9 earthquake, Lisbon's 1755 quake, Krakatoa's 1883 eruption, and the devastating Sumatra 2004 quake created similarly catastrophic tsunamis. Survey the terrain of megatsunamis, and learn potential future tsunami triggers.

The Eruption of Vesuvius and the Impact of Volcanoes — The term "Plinian volcanic eruptions" honors Pliny the Younger who chronicled the 79 CE eruption of Vesuvius. These eruptions eject ash high in the atmosphere, having their greatest impact through global climate change. From Peru to Russia, from eruptions 74,000 BCE to the French Revolution, you'll focus on the impact of volcanos on history. Time well spent with Dr. Wysession, who keeps his eye on the Yellowstone Caldera!

Fermi's Paradox and the Likelihood of Finding Another Earth — During a discussion on the likelihood of intelligent civilizations existing elsewhere, the physicist Enrico Fermi asked "Well, where is everybody?" Geologic research shows that the conditions required for life to exist continuously for nearly four billion years are stringent, and may rarely occur in the galaxy. Learn all of the factors that had to happen just right to produce Earth's spectacular and potentially unique diversity of geologic and biologic environments.

SCIENTIFIC AMERICAN Travel HIGHLIGHTS

ISTANBUL TOUR

It's impossible to describe, and has mesmerized travelers for millennia. Layered,amalgamated, flowing. Ancient and modern, secular and sacred. Plunge into Istanbul's cultural whirlwind with Bright Horizons staff, who have been there, done that.

On your itinerary: Hagia Sophia. It was the largest cathedral in the world for a thousand years, then a mosque, now a secular museum (so Istanbul). The Blue Mosque is defined by its 20,000 Iznik tiles. We'll peruse the sweets, spices, and nuts at the Spice Bazaar (A little hazelnut-pomegranate nougat, perhaps?).

Onward to our learning lab in Turkish hospitality, doing lunch at Topkapi Palace's former guard house. Then we'll immerse ourselves in the context and treasures of Topkapi, including the Treasury, Harem, and Holy Relics sections. Risking total sensory overload, we'll conclude our day at the Istanbul Archaeology Museum. Price: $119.

ATHENS' BEST

Visit the new Acropolis Museum and the National Archaeological Museum with our skilled guide who will add immeasurably to your experience. See the Parthenon frieze, exquisite sanctuary relics, and Archaic sculpture at the Acropolis Museum. Lunch, of course, is tucked away at a taverna favored by Athenian families. For dessert, we'll visit the richest array of Greek antiquties anywhere at the National Archaeological Museum. Price: $135.

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Many civilizations left their mark at Ephesus. It's a many layered, many splendored history, often oversimplfied. Bright Horizons pulls together three important elements of Ephesus rarely presented together. Meander the Marble Road, visit the legendary latrines, check out the Library, and visit the centers of the city. A visit to the Terrace Houses enlivens your picture of Roman Ephesus. Lunch on Mediterranean cuisine in the countryside, and then visit the Ephesus Museum where you get a fuller look at local history, from the Lydians to the Byzantines. Price: $105.

PRIVATE, INSIDER'S TOUR OF CERN

September 27, 9am–4pm — From the tiniest constituents of matter to the immensity of the cosmos, discover the wonders of science and technology at CERN. Join Bright Horizons for a private pre-cruise, custom, full-day tour of this iconic facility.

This trip is limited to 50 people. For questions and hotel pricing, please contact Neil or Theresa, or give us a call at (650) 787-5667.

Our full day will be led by a CERN official and physicist. We'll have an orientation; visit an accelerator and experiment; get a sense of the mechanics of the large hadron collider (LHC); and have time to peruse exhibits and media on the history of CERN and the nature of its work.

To take advantage of this unrivaled insider access to CERN, rendezvous on September 27, 2011 in Geneva, Switzerland. The price is $299 and includes lunch at CERN and a round-trip transfer from our Geneva hotel to CERN.

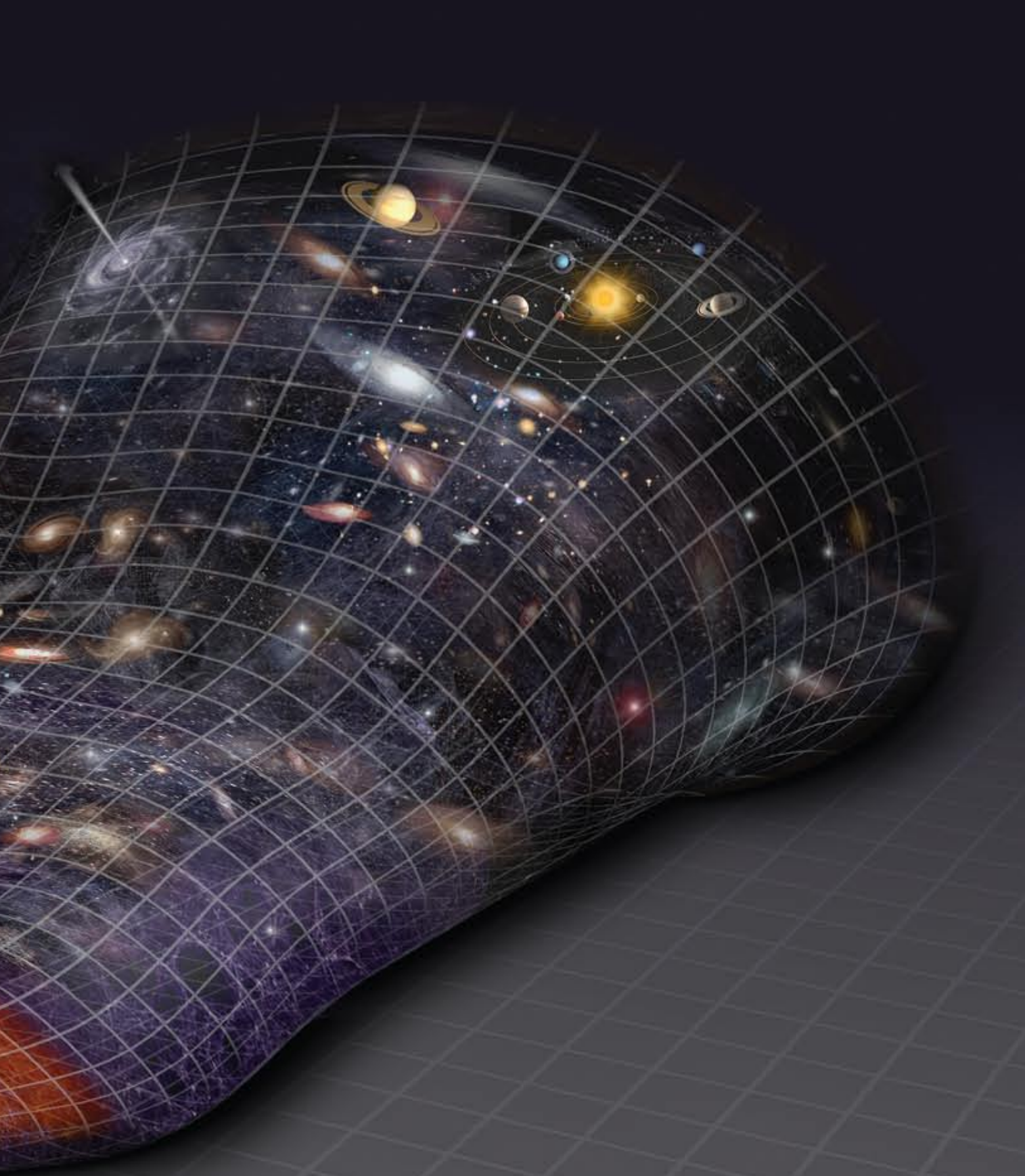
COSMOLOGY

The Inflation Debate

Is the theory at the heart of modern cosmology deeply flawed?

By Paul J. Steinhardt

Illustrations by Malcolm Godwin



Deflating cosmology? Cosmologists are reconsidering whether the universe really went through an intense growth spurt (*yellowish region*) shortly after the big bang.

Paul J. Steinhardt is director of the Princeton Center for Theoretical Science at Princeton University. He is a member of the National Academy of Sciences and received the P.A.M. Dirac Medal from the International Center for Theoretical Physics in 2002 for his contributions to inflationary theory. Steinhardt is also known for postulating a new state of matter known as quasicrystals.

THIRTY YEARS AGO ALAN H. GUTH, THEN A STRUGGLING PHYSICS postdoc at the Stanford Linear Accelerator Center, gave a series of seminars in which he introduced "inflation" into the lexicon of cosmology. The term refers to a brief burst of hyperaccelerated expansion that, he argued, may have occurred during the first instants after the big bang. One of these seminars took place at Harvard University, where I myself was a postdoc. I was immediately captivated by the idea, and I have been thinking about it almost every day since. Many of my colleagues working in astrophysics, gravitational physics and particle physics have been similarly engrossed. To this day the development and testing of the inflationary theory of the universe is one of the most active and successful areas of scientific investigation.

Its raison d'être is to fill a gap in the original big bang theory. The basic idea of the big bang is that the universe has been slowly expanding and cooling ever since it began some 13.7 billion years ago. This process of expansion and cooling explains many of the detailed features of the universe seen today, but with a catch: the universe had to start off with certain properties. For instance, it had to be extremely uniform, with only extremely tiny variations in the distribution of matter and energy. Also, the universe had to be geometrically flat, meaning that curves and warps in the fabric of space did not bend the paths of light rays and moving objects.

But why should the primordial universe have been so uniform and flat? A priori, these starting conditions seemed unlikely. That is where Guth's idea came in. He argued that even if the universe had started off in total disarray—with a highly nonuniform distribution of energy and a gnarled shape—a spectacular growth spurt would have spread out energy until it was evenly dispersed and straightened out any curves and warps in space. When this period of inflation ended, the universe would have continued to expand at the more mellow pace of the original big bang theory but now with just the right conditions for stars and galaxies to evolve to the state where we see them today.

The idea is so compelling that cosmologists, including me, routinely describe it to students, journalists and the public as an established fact. Yet something peculiar has happened to inflationary theory in the 30 years since Guth introduced it. As the case for inflation has grown stronger, so has the case against. The two cases are not equally well known: the evidence favoring inflation is familiar to a broad range of physicists, astrophysicists and science aficionados. Surprisingly few seem to follow the case against inflation except for a small group of us who have been quietly striving to address the challenges. Most astrophysicists have gone about their business testing the predictions of textbook inflationary theory without worrying about these deeper issues, hoping they would eventually be resolved. Unfortunately, the problems have resisted our best efforts to date.

As someone who has contributed both to inflationary theory [see "The Inflationary Universe," by Alan H. Guth and Paul J. Steinhardt; SCIENTIFIC AMERICAN, May 1984] and to competing theories, I feel torn, and I sense that many of my colleagues are not sure what to make of the case against, either. To dramatize our strange predicament, I will place inflationary cosmology on trial, presenting the two extreme points of view. First, I will act as fervent advocate "for," presenting the strongest advantages of the theory, and then, with equal fervor, as advocate "against," presenting the most serious unresolved problems.

THE CASE FOR INFLATION

INFLATION is so well known that the case for it can be brief. A few more details are necessary to appreciate its advantages fully. Inflation relies on a special ingredient known as inflationary energy, which, combined with gravity, can drive the universe to expand by an astonishing amount over a brief instant. The inflationary energy must be hugely dense, and its density must remain nearly constant during the inflationary epoch. Its most unusual property of all is that its gravity must repel rather than attract. The repulsion is what causes space to swell so rapidly.

What gave Guth's idea its appeal was that theorists had already identified many possible sources of such energy. The leading example is a hypothesized relative of the magnetic field known as a scalar field, which, in the particular case of inflation,

IN BRIEF

Cosmic inflation is so widely accepted that it is often taken as established fact. The idea is that the geometry and uniformity of the cosmos were established during an intense early growth spurt.

But some of the theory's creators, including the author, are having second thoughts. As the original theory has developed, cracks have appeared in its logical foundations.

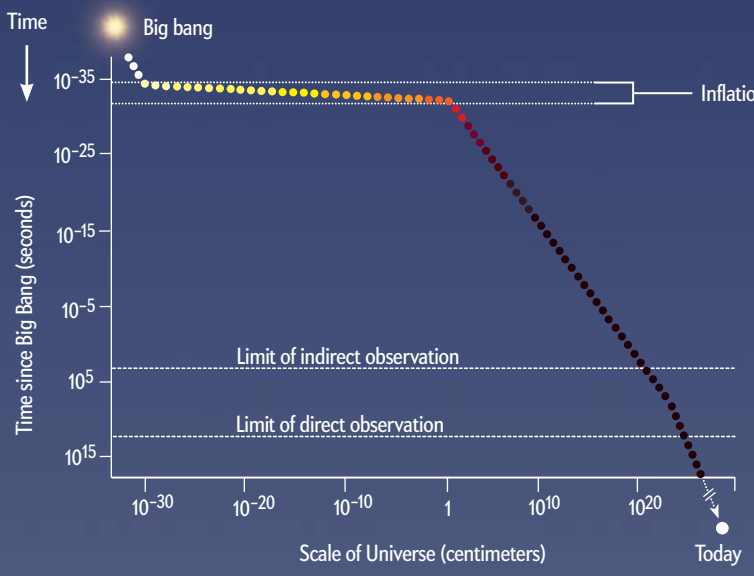
Highly improbable conditions are required to start inflation. Worse, inflation goes on eternally, producing infinitely many outcomes, so the theory makes no firm observational predictions.

Scientists debate among (and within) themselves whether these troubles are teething pains or signs of a deeper rot. Various proposals are circulating for ways to fix inflation or replace it.

The Ultimate Growth Spurt

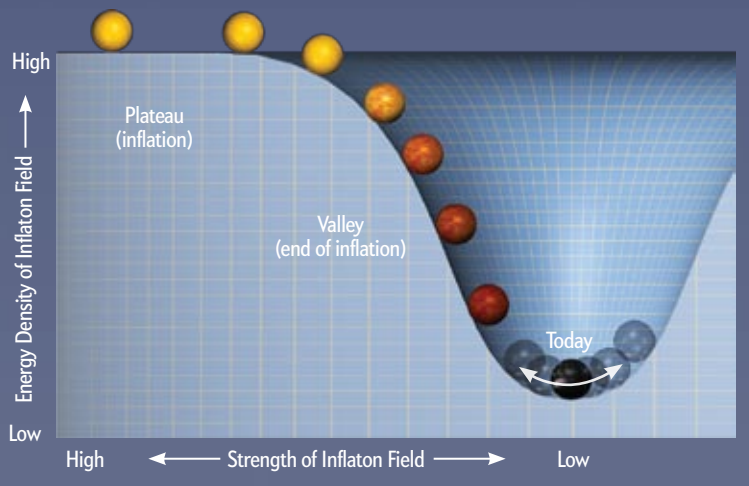
Astronomers observe that the universe is expanding and has been doing so for 13.7 billion years. But what happened at the very earliest times, too early to see directly? The leading idea is known as cosmic inflation. It supposes that the embryonic universe abruptly ballooned in size. Such a growth spurt would have ironed out any curves and warps in space, thus explaining the geometry of the universe today, and left behind slight nonuniformities that seeded galaxies.

WHAT INFLATION DID

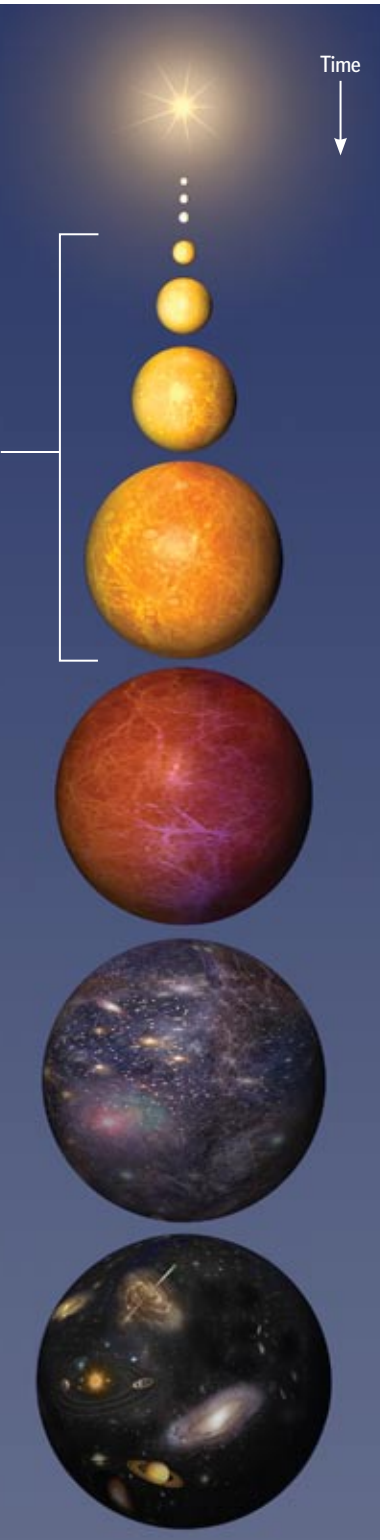


The amount of growth was impressive even by astronomers' standards. Within 10^{-30} second, the universe enlarged by a factor of at least 10^{25} in every direction. It expanded at an accelerated rate, pulling regions of space apart faster than the speed of light.

WHAT CAUSED INFLATION



A relative of the magnetic field, the "inflaton" generated a repulsive gravitational force that drove space to swell rapidly momentarily. For that to occur, the field's energy density had to vary with strength such that it had a high-energy plateau and a low-energy valley. The field evolved like a ball rolling downhill. On the plateau, it exerted the repulsive force. When it hit the valley, inflation ended.



The volume of space we observe today was a quadrillionth the size of an atom when inflation began. During inflation it grew to the size of a dime. In the billions of years since then, space has continued to expand but at a mellower pace, allowing structures such as galaxies to form. (This figure is conceptual and not to scale.)

Graphic by Jen Christiansen (top left)

is known as the "inflaton" field. The famous Higgs particle now being sought at CERN's Large Hadron Collider near Geneva derives from another scalar field.

Like all fields, the inflaton has a certain strength at every point in space, which determines the force it exerts on itself and on other fields. During the inflationary phase, its strength is nearly constant everywhere. Depending on how strong a field is, it has a certain amount of energy in it—what physicists call potential energy. The relation between the strength and the energy can be represented by a curve on a graph. For the inflaton, cosmologists hypothesize that the curve looks like the cross section through a valley and a gently sloped plateau [*see box on preceding page*]. If the field begins with a strength corresponding to some point on the plateau, it will gradually lose both strength and energy, as if sliding down the slope. In fact, the equations are similar to those of a ball rolling down a hill of the same shape as the potential energy curve.

The inflaton's potential energy can cause the universe to expand at an accelerated rate. In the process, it can smooth and flatten the universe, provided the field remains on the plateau long enough (about 10^{-30} second) to stretch the universe by a factor of 10^{25} or more along each direction. Inflation ends when the field reaches the end of the plateau and rushes downhill to the energy valley below. At this point, the potential energy converts into more familiar forms of energy—namely, the dark matter, hot ordinary matter and radiation that fill the universe today. The universe enters a period of modest, decelerating expansion during which the material coalesces into cosmic structures.

Inflation smoothes the universe just as stretching a rubber sheet smoothes its wrinkles, but it does not do so perfectly. Small irregularities remain because of quantum effects. The laws of quantum physics dictate that a field such as the inflaton not have exactly the same strength everywhere in space but that it undergo random fluctuations. These fluctuations cause inflation to end at slightly different times in different regions of space, heating them to slightly different temperatures. These spatial variations are the seeds that will eventually grow into stars and galaxies. A prediction of inflationary theory is that the variations are nearly scale-invariant. That is, they do not depend on the size of the region; they occur with equal magnitude on all scales.

The case for inflation can be summarized by three dictums. First, inflation is inevitable. Developments in theoretical physics since Guth's proposal have only strengthened the hypothesis that the early universe contained fields that could conceivably drive inflation. Hundreds of them appear in unified theories of physics, such as string theory. In the chaotic primeval universe, there was sure to be some patch of space where one of these fields met the conditions for inflation.

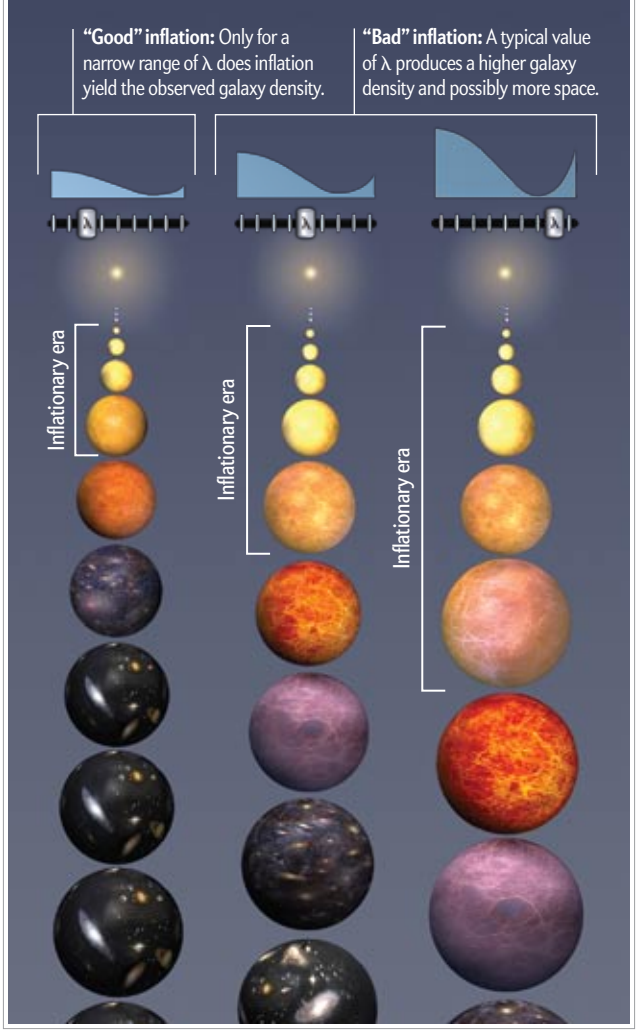
Second, inflation explains why the universe is so uniform and flat today. No one knows how uniform or flat the universe was when it emerged from the big bang, but with inflation there is no need to know because the period of accelerated expansion stretched it into the right shape.

Third, and probably the most compelling, inflationary theory is powerfully predictive. For example, numerous observations of the cosmic microwave background radiation and the distribution of galaxies have confirmed that the spatial variations in energy in the early universe were nearly scale-invariant.

PROBLEM #1: "BAD" INFLATION

Unlikely to Be Good

Inflation was supposed to create a huge volume of space matching the observed large-scale features of our universe naturally. But unless the inflaton energy curve had a very specific shape (obtained by finely tuning one or more parameters, abbreviated λ here), the outcome would be "bad"—a huge volume with too high a density and the wrong distribution of galaxies. Given the range of possible λ values, bad inflation seems more likely.



THE CASE AGAINST INFLATION

THE FIRST SIGNS that a theory is failing are usually small discrepancies between observations and predictions. That is not the situation here: the data are in exquisite accord with the inflationary predictions set down in the early 1980s. Instead the case against inflation challenges the logical foundations of the theory. Does the theory really work as advertised? Are the predictions made in the early 1980s still the predictions of the inflationary model as we understand it today? There is an argument to be made that the answer to both questions is no.

The first dictum holds that inflation is inevitable. But if it is, there is an awkward corollary: bad inflation is more likely than good inflation. "Bad inflation" means a period of accelerated ex-

pansion whose outcome conflicts with what we observe. For example, the temperature variations might be too large. The difference between good and bad hinges on the precise shape of the potential energy curve, which is controlled by a numerical parameter that could, in principle, take on any value whatsoever. Only an extremely narrow range of values could produce the observed temperature variation. In a typical inflationary model, the value must be near 10^{-15}—that is, zero to 15 decimal places. A less fine-tuned choice, such as zero to only 12 or 10 or eight decimal places, would produce bad inflation: the same degree of accelerated expansion (or more) but with a large temperature variation that is inconsistent with observations.

We could ignore bad inflation if it were incompatible with life. In that case, even if such large temperature variations could arise in principle, we could never observe them. Reasoning of this kind is known as the anthropic principle. Yet it does not apply here. Larger temperature variations would result in more stars and galaxies—the universe would, if anything, be more habitable than it is now.

Not only is bad inflation more likely than good inflation, but no inflation is more likely than either. University of Oxford physicist Roger Penrose first made this point in the 1980s. He applied thermodynamic principles, similar to those used to describe configurations of atoms and molecules in a gas, to count the possible starting configurations of the inflaton and gravitational fields. Some of these configurations lead to inflation and thence to a nearly uniform, flat distribution of matter and a geometrically flat shape. Other configurations lead to a uniform, flat universe directly—without inflation. Both sets of configurations are rare, so obtaining a flat universe is unlikely overall. Penrose's shocking conclusion, though, was that obtaining a flat universe without inflation is much more likely than with inflation—by a factor of 10 to the googol (10^{100}) power!

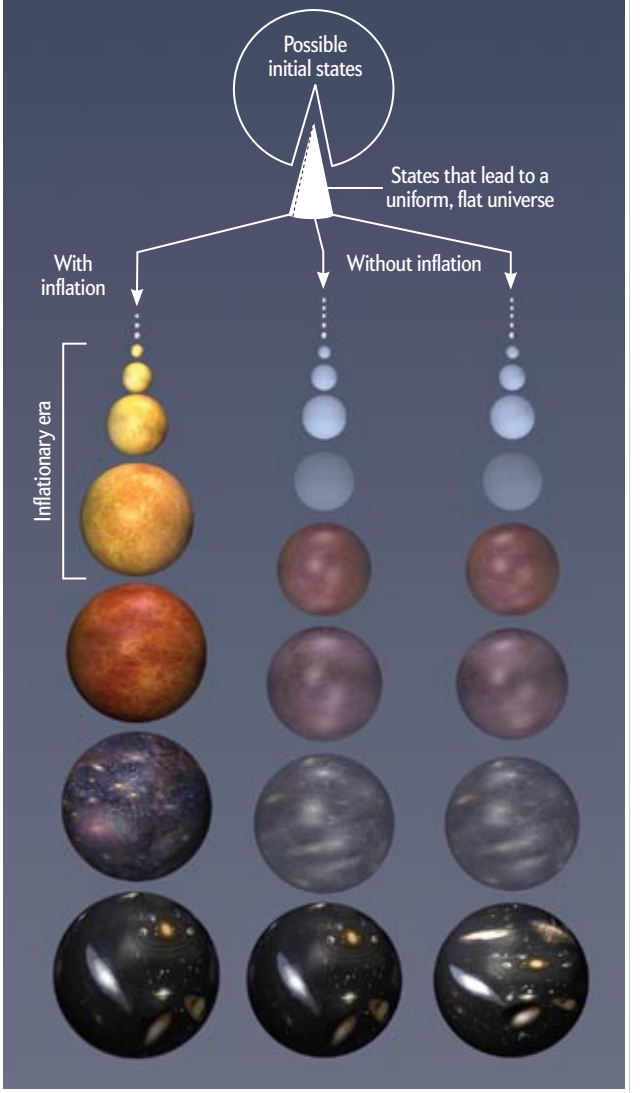
THE PERILS OF AN ETERNAL INFLATION

ANOTHER APPROACH reaching a similar conclusion extrapolates the history of the universe from its current conditions backward in time using the established physical laws. The extrapolation is not unique: given the average flat and smooth conditions today, many different sequences of events could have come before. In 2008 Gary W. Gibbons of the University of Cambridge and Neil G. Turok of the Perimeter Institute for Theoretical Physics in Ontario showed that an overwhelming number of extrapolations have insignificant amounts of inflation. This conclusion is consistent with Penrose's. Both seem counterintuitive because a flat and smooth universe is unlikely, and inflation is a powerful mechanism for obtaining the needed smoothing and flattening. Yet this advantage appears to be completely offset by the fact that the conditions for starting inflation are so improbable. When all factors are taken into account, the universe is more likely to have achieved its current conditions without inflation than with it.

Many physicists and astrophysicists find these theoretical arguments unconvincing compared with a more compelling one favoring inflation: namely, the agreement between the predictions formulated in the early 1980s and the magnificent cosmological observations available today. Matching experiments trumps any theoretical argument. But the strange twist to this story is that the predictions of the early 1980s were based on a naive understanding of how inflation actually works—a picture that has turned out to be dead wrong.

It Had to Be Just So

Inflation was supposed to occur no matter what the initial conditions of the universe were. Further analysis suggests otherwise. Of all the ways the universe could have begun, only a tiny fraction would lead to the uniform, flat state observed today. An overwhelming fraction of these would reach this state without significant inflation; only an infinitesimal fraction would do so by going through a long period of inflation.



The change in view began with the realization that inflation is eternal: once begun, it never ends [see "The Self-Reproducing Inflationary Universe," by Andrei Linde; SCIENTIFIC AMERICAN, November 1994]. The self-perpetuating nature of inflation is the direct result of quantum physics combined with accelerated expansion. Recall that quantum fluctuations can slightly delay when inflation ends. Where these fluctuations are small, so are their effects. Yet the fluctuations are uncontrollably random. In some regions of space, they will be large, leading to substantial delays.

Such procrastinating rogue regions are extremely rare, so you might think it safe to ignore them. You cannot, because they are

inflating. They continue to grow and, in a matter of instants, dwarf the well-behaved region that ended inflation on time. The result is a sea of inflating space surrounding a little island filled with hot matter and radiation. What is more, rogue regions spawn new rogue regions, as well as new islands of matter—each a self-contained universe. The process continues ad infinitum, creating an unbounded number of islands surrounded by ever more inflating space. If you are not disturbed by this picture, don't worry—you should not be. The disturbing news comes next.

The islands are not all the same. The inherently random nature of quantum physics ensures that some are highly nonuniform or strongly warped. Their nonuniformity sounds like the problem of bad inflation described earlier, but the cause is different. Bad inflation occurs because the parameters controlling the shape of the potential energy curve are likely to be too large. Here nonuniformity can result from eternal inflation and random quantum fluctuations no matter what values the parameters have.

To be quantitatively precise, the word "some" above should be replaced with "an infinite number of." In an eternally inflating universe, an infinite number of islands will have properties like the ones we observe, but an infinite number will not. The true outcome of inflation was best summarized by Guth: "In an eternally inflating universe, anything that can happen will happen; in fact, it will happen an infinite number of times."

So is our universe the exception or the rule? In an infinite collection of islands, it is hard to tell. As an analogy, suppose you have a sack containing a known finite number of quarters and pennies. If you reach in and pick a coin randomly, you can make a firm prediction about which coin you are most likely to choose. If the sack contains an infinite number of quarter and pennies, though, you cannot. To try to assess the probabilities, you sort the coins into piles. You start by putting one quarter into the pile, then one penny, then a second quarter, then a second penny, and so on. This procedure gives you the impression that there is an equal number of each denomination. But then you try a different system, first piling 10 quarters, then one penny, then 10 quarters, then another penny, and so on. Now you have the impression that there are 10 quarters for every penny.

Which method of counting out the coins is right? The answer is neither. For an infinite collection of coins, there are an infinite number of ways of sorting that produce an infinite range of probabilities. So there is no legitimate way to judge which coin is more likely. By the same reasoning, there is no way to judge which kind of island is more likely in an eternally inflating universe.

Now you should be disturbed. What does it mean to say that inflation makes certain predictions—that, for example, the universe is uniform or has scale-invariant fluctuations—if anything that can happen will happen an infinite number of times? And if the theory does not make testable predictions, how can cosmologists claim that the theory agrees with observations, as they routinely do?

THE MEASURE OF OUR FAILURE

THEORISTS ARE NOT UNAWARE of the problem, but they have faith that they can resolve it and restore the naive inflationary picture of the early 1980s that attracted them to the theory in the first place. Many remain hopeful even though they have been wrestling with this issue for the past 25 years and have yet to come up with a plausible solution.

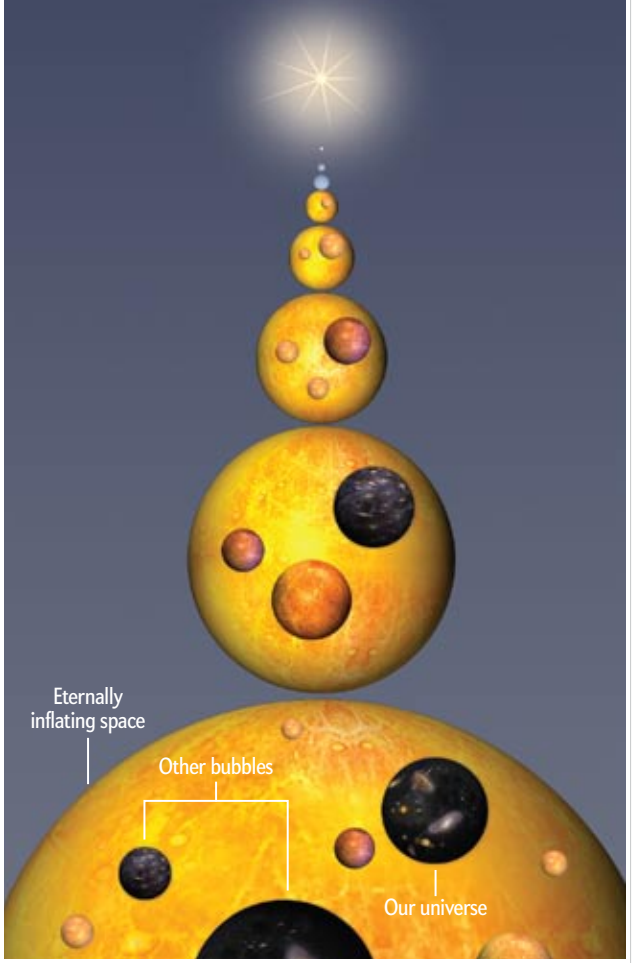
Some suggest trying to construct theories of inflation that are not eternal, to nip the infinity of universes in the bud. But eternality is a natural consequence of inflation plus quantum physics. To avoid it, the universe would have to start off in a very special initial state and with a special form of inflationary energy, so that inflation ended everywhere in space before quantum fluctuations had a chance to reignite it. In this scenario, though, the observed outcome depends sensitively on what the initial state is. That defeats the entire purpose of inflation: to explain the outcome no matter what conditions existed beforehand.

An alternative strategy supposes that islands like our observable universe are the most likely outcome of inflation. Proponents of this approach impose a so-called measure, a specific rule for weighting which kinds of islands are most likely—analogous to declaring that we must take three quarters for every five pennies when drawing coins from our sack. The notion of a

PROBLEM #3: ETERNAL INFLATION

The Abyss of Infinity

Inflation is known for making precise predictions that have been confirmed by observations. But does it really? Once inflation starts, quantum jittering keeps it going in the bulk of space. Where it does end, a bubble nucleates and grows. We live in such a bubble, but it is atypical; most are younger. In fact, an infinite number of bubbles form with an infinite variety of properties. Everything that can happen does happen in some bubble. A theory that predicts everything predicts nothing.



measure, an ad hoc addition, is an open admission that inflationary theory on its own does not explain or predict anything.

Worse, theorists have come up with many equally reasonable measures that lead to different conclusions. An example is the volume measure, which says that islands should be weighted by their size. At first glance, this choice makes common sense. The intuitive idea underlying inflation is that it explains the uniformity and flatness we observe by creating large volumes of space with those properties. Unfortunately, the volume measure fails. The reason is that it favors procrastination. Consider two kinds of regions: islands like ours and others that formed later, after more inflation. By the power of exponential growth, the latter regions will occupy vastly more total volume. Hence, regions younger than ours are vastly more common. By this measure, it is unlikely we would even exist.

Measure enthusiasts take a trial-and-error approach in which they invent and test measures until, they hope, one produces the desired answer: that our universe is highly probable. Suppose they succeed someday. Then they will need another principle to justify using that measure instead of the others, yet another principle to choose that principle, and so on.

Still another alternative approach is to invoke the anthropic principle. Whereas the measure concept holds that we live in a typical island, the anthropic principle assumes we live in a very atypical island with just the minimal conditions needed to support life. The claim is that the conditions in more typical islands are incompatible with galaxies or stars or some other prerequisite for life as we know it. Even though the typical islands occupy more space than ones like ours, they can be ignored because we are interested only in regions that humans could potentially inhabit.

MORE ON COSMIC INFLATION
ScientificAmerican.com/apr2011/inflation

Unfortunately for this idea, the conditions in our universe are not minimal—the universe is flatter, smoother and more precisely scale-invariant than it had to be to support life. More typical islands, such as those younger than ours, are almost equally habitable yet much more numerous.

MAKING PROCRASTINATORS PAY

IN LIGHT OF THESE ARGUMENTS, the oft-cited claim that cosmological data have verified the central predictions of inflationary theory is misleading, at best. What one can say is that data have confirmed predictions of the naive inflationary theory as we understood it before 1983, but this theory is not inflationary cosmology as understood today. The naive theory supposes that inflation leads to a predictable outcome governed by the laws of classical physics. The truth is that quantum physics rules inflation, and anything that can happen will happen. And if inflationary theory makes no firm predictions, what is its point?

The underlying problem is that procrastination carries no penalty—to the contrary, it is positively rewarded. Rogue regions that delay ending inflation continue to grow at an accelerating pace, so they invariably take over. In an ideal situation, any rogue regions would expand more slowly—or, better still, shrink. The overwhelming bulk of the universe would consist of well-behaved regions that end the smoothing phase on time, and our observed universe would be comfortably normal.

An alternative to inflationary cosmology that my colleagues and I have proposed, known as the cyclic theory, has just this property. According to this picture, the big bang is not the beginning of space and time [see "The Myth of the Beginning of Time," by Gabriele Veneziano; SCIENTIFIC AMERICAN, May 2004] but rather a "bounce" from a preceding phase of contraction to a new phase of expansion, accompanied by the creation of matter and radiation. The theory is cyclic because, after a trillion years, the expansion devolves into contraction and a new bounce to expansion again. The key point is that the smoothing of the universe occurs before the bang, during the period of contraction. Any procrastinating rogue regions continue to contract while well-behaved regions bounce on time and begin expanding, so the rogue regions remain comparatively small and negligible.

Smoothing during contraction has an observable consequence. During any smoothing phase, whether in inflationary theory or in the cyclic theory, quantum fluctuations generate small, propagating random distortions in spacetime, known as gravitational waves, that leave a distinctive imprint on the microwave background radiation. The amplitude of the waves is proportional to the energy density. Inflation would occur when the universe was extremely dense, whereas the equivalent process in the cyclic model would occur when the universe was practically empty, so the predicted imprints would be dramatically different. Of course, the cyclic theory is relatively new and may have its own problems, but it illustrates that there are conceivable alternatives that may not suffer the uncontrollable runaway of eternal inflation. Our preliminary work suggests the cyclic model avoids the other problems described earlier, too.

To be sure, I have presented the cases for and against inflation as two extremes without the opportunity for cross-examination or nuance. In a meeting held in January at the Princeton Center for Theoretical Science to discuss these issues, many leading theorists argued that the problems with inflation are mere teething pains and should not shake our confidence in the basic idea. Others (including me) contended that the problems cut to the core of the theory, and it needs a major fix or must be replaced.

In the end, the case will be decided by data. The forthcoming observations of the microwave background radiation will be telling. Experiments to search for a gravitational-wave imprint are already being conducted on mountaintops, in high-altitude balloons and onboard satellites, and results should emerge within the next two to three years. Detecting a gravitational-wave imprint would support inflation; failure to detect it would be a major setback. For inflation to make sense despite a null result, cosmologists would need to suppose that the inflaton field had a very peculiar potential with just the right shape to suppress gravitational waves, which seems contrived. Many researchers would gravitate to alternatives, like the cyclic universe theory, that naturally predict an unobservably small gravitational-wave signal. The outcome will be a critical moment in our quest to determine how the universe came to be the way it is and what will happen to it in the future. SA

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~Dr. George Barclay
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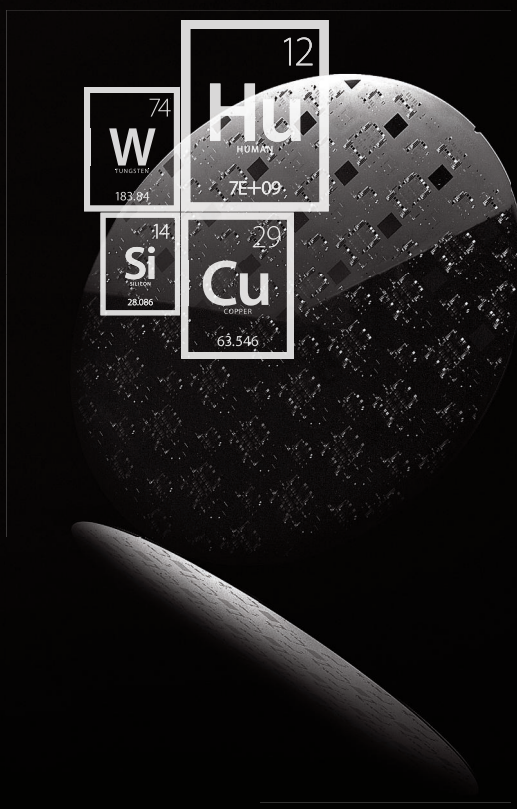


MEDICINE

The Enemy Within

A new pattern of antibiotic resistance that is spreading around the globe may soon leave us defenseless against a frighteningly wide range of dangerous bacterial infections

By Maryn McKenna

Photograph by Darren Braun

Maryn McKenna is an independent science journalist and a blogger for *Wired*. She has reported from the scene of disease outbreaks on most of the continents. She is author of *Superbug: The Fatal Menace of MRSA* (Free Press, 2010) and *Beating Back the Devil: On the Front Lines with the Disease Detectives of the Epidemic Intelligence Service* (Free Press, 2004).

IN EARLY SUMMER 2008 TIMOTHY WALSH OF CARDIFF UNIVERSITY IN WALES GOT AN e-mail from Christian Giske, an acquaintance who is a physician on the faculty of Sweden's Karolinska Institute. Giske had been treating a 59-year-old man hospitalized that past January in Örebro, a small city about 100 miles from Stockholm. The man had lived with diabetes for many years, suffered several strokes and had lately developed deep bedsores. But those were not the subject of Giske's message. Instead he was worried about a bacterium that a routine culture had unexpectedly revealed in the man's urine. Would Walsh, who runs a lab that unravels the genetics of antibacterial resistance, be willing to take a look at the bug?

Walsh agreed and put the isolate through more than a dozen assays. It was *Klebsiella pneumoniae,* a bacterium that in hospitalized patients is one of the most frequent causes of pneumonia and bloodstream infection. This strain, though, contained something new, a gene that Walsh had never seen before. It rendered the *Klebsiella,* which was already resistant to many antibiotics used in critical care medicine, insensitive to the only remaining group that worked reliably and safely—the carbapenems, the so-called drugs of last resort. The one medication the investigators found that had any effect on the resistant strain was colistin, a drug that had been out of general use for years because of its toxic effects on the kidneys. Walsh named the enzyme that this gene produced New Delhi metallo-beta-lactamase, or NDM-1, for the city where the man acquired the infection just before he returned home to Sweden.

If there was one such case, Walsh thought, there were likely to be others—and he, Giske and a team of collaborators went in search of them. In August 2010 they published their results in *Lancet Infectious Diseases:* they had found 180 instances of patients carrying the gene. NDM-1 was widely distributed in *Klebsiella* in India and Pakistan and had already traveled to the U.K. via residents who had traveled to South Asia for medical care or to visit friends and family. Worse, it had spread in a few cases into a different bacterial genus—from *Klebsiella* into *Escherichia coli,* which lives in the gut of every warm-blooded being and is ubiquitous in our environment. That transfer raised the prospect that the gene would not stay confined to hospitals and hospital infections but would begin moving silently through the everyday world, carried in bacteria in the intestines of average people, advancing without detection via handshakes and kisses and doorknobs.

It raised another possibility as well: that the delicate, seesawing balance between bugs and drugs, set into motion in 1928 with the discovery of penicillin, was about to come down for good on the side of the bacteria. If so, many lethal infections that antibiotics have held at bay for decades might soon return with a vengeance.

A NEW PATTERN OF RESISTANCE

THE END of the antibiotic miracle is not a new theme. For as long as there have been antibiotics, there has been antibiotic resistance: the first penicillin-resistant bacteria surfaced before penicillin was even released to the marketplace in the 1940s. And for almost that long, doctors have raised the alarm over running out of drugs, sparked by the global spread of penicillin-resistant organisms in the 1950s and followed by methicillin resistance in the 1980s and vancomycin resistance in the 1990s.

This time, though, the prediction of postantibiotic doom comes from a different part of the microbial world. The genes that confer carbapenem resistance—not just NDM-1, but an alphabet soup of others—have appeared over the past decade or so in a particularly challenging grouping of bacteria called gram-negatives. That designation, which borrows the name of a Danish 19th-century scientist, superficially indicates the response to a stain that illuminates the cell membrane. What it connotes is

IN BRIEF

A new pattern of resistance has emerged among a particularly challenging group of bacteria called the gram-negatives; it threatens to make many common infections untreatable.

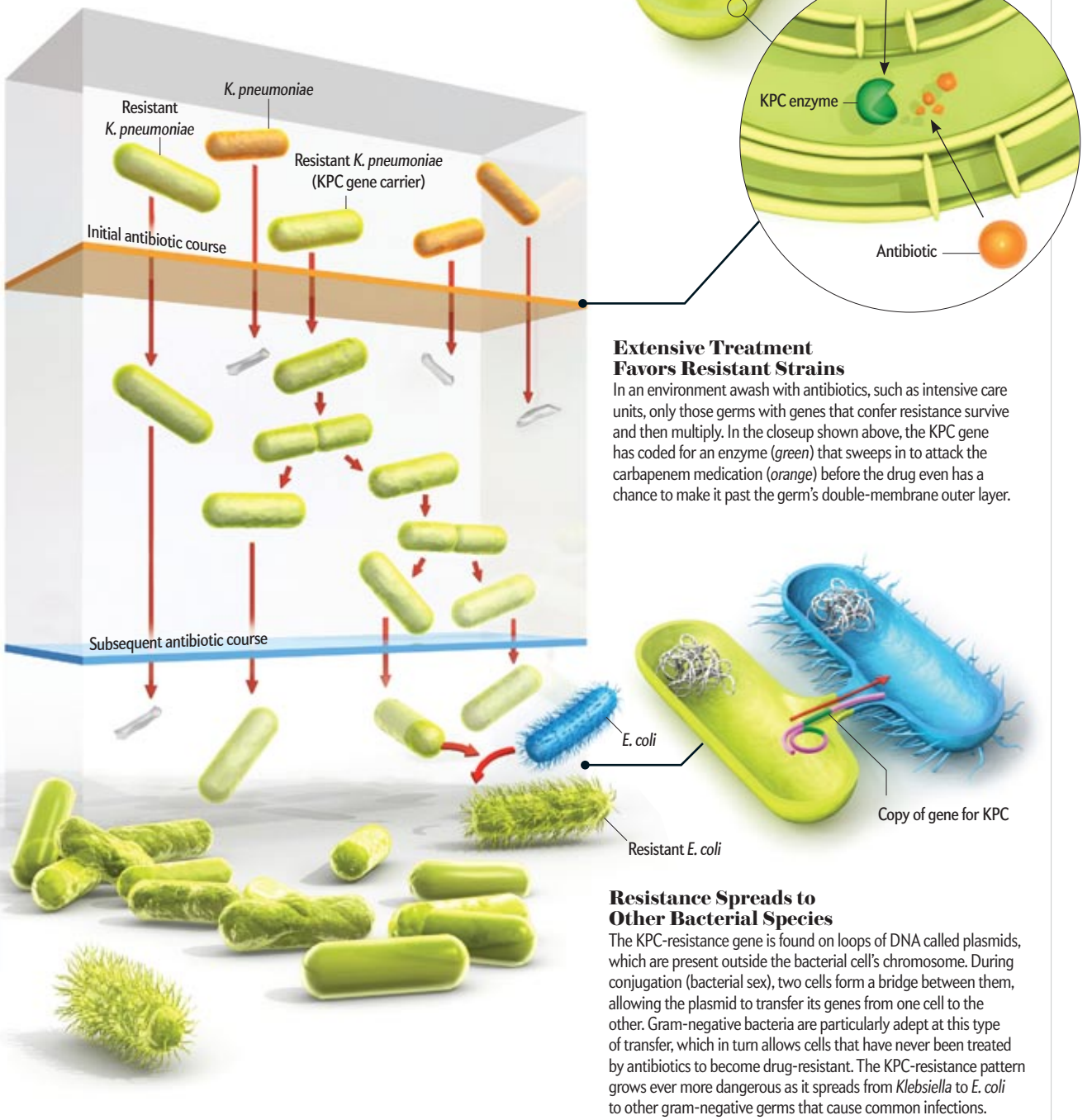
The bacterial genes responsible confer resistance to the carbapenems, a group of so-called last-resort antibiotics. Two of the most important resistance genes are dubbed NDM-1 and KPC.

Carbapenem resistance in gram-negative bacteria is especially worrisome because these germs are ubiquitous and share genes easily. Plus, no new drugs for these bugs are being developed.

This confluence of factors means many people in hospitals and in the wider community could die of newly untreatable infections of the urinary tract, blood and other tissues.

Resistance Roulette

The constant use of antibiotics, which helps to foster drug resistance across bacterial species, has produced a deadly new threat. The new strain, depicted below, began with a few *Klebsiella* bacteria that happened to carry the KPC gene, which rendered them insensitive to antibiotics known as carbapenems. Multiple rounds of ineffective treatment cleared the way for the KPC-bearing bacteria to proliferate. Even more worrisome, as shown on the right, *Klebsiella* and other gram-negative bacteria easily share KPC- and other resistance genes across species, which could make them impermeable to all drugs.



Extensive Treatment Favors Resistant Strains

In an environment awash with antibiotics, such as intensive care units, only those germs with genes that confer resistance survive and then multiply. In the closeup shown above, the KPC gene has coded for an enzyme (*green*) that sweeps in to attack the carbapenem medication (*orange*) before the drug even has a chance to make it past the germ's double-membrane outer layer.

Resistance Spreads to Other Bacterial Species

The KPC-resistance gene is found on loops of DNA called plasmids, which are present outside the bacterial cell's chromosome. During conjugation (bacterial sex), two cells form a bridge between them, allowing the plasmid to transfer its genes from one cell to the other. Gram-negative bacteria are particularly adept at this type of transfer, which in turn allows cells that have never been treated by antibiotics to become drug-resistant. The KPC-resistance pattern grows ever more dangerous as it spreads from *Klebsiella* to *E. coli* to other gram-negative germs that cause common infections.

Illustration by Bryan Christie

much more complex. Gram-negative bacteria are promiscuous: they easily exchange bits of DNA, so that a resistance gene that arises in *Klebsiella,* for example, quickly migrates to *E. coli, Acinetobacter* and other gram-negative species. (In contrast, resistance genes in gram-positives are more likely to cluster within species.) Gram-negative germs are also harder to kill with antibiotics because they have a double-layered membrane that even powerful drugs struggle to penetrate and possess certain internal cellular defenses as well. In addition, fewer options exist for treating them. Pharmaceutical firms are making few new antibiotics of any type these days. Against the protean, stubborn gram-negatives, they have no new compounds in the pipeline at all. All told, this unlucky confluence of elements could easily export disaster from medical centers to the wider community.

Resistance to the carbapenem class of antibiotics has already brought hospital-acquired infections, such as the *Klebsiella* that infected that original Swedish patient, to the brink of untreatability. Beyond the carbapenems, there remain only a few drugs that doctors are loathe to prescribe, either because they cannot reach all the hiding places in the body where bacteria dwell or they make patients so sick as to be unsafe.

Even if health care–related infections are difficult to cure, they are usually detected because the patients in whom they occur—elderly, debilitated, confined to an intensive care unit—are usually under close watch. What keeps health authorities awake at night is the possibility that carbapenem-resistance genes will propagate, undetected, beyond the hospital inside of organisms that cause everyday maladies—such as *E. coli,* which is responsible for most of the millions of urinary tract infections in the U.S. every year. Walsh, NDM-1's discoverer, proffers the example of a woman dropping in to see her primary care doctor with what looks like uncomplicated cystitis. With no reason to suspect resistance, the physician would prescribe drugs that no longer work, while the infection spread unimpeded up her urinary tract, into her kidneys and, devastatingly, into her blood. "There would be nothing to treat her with," he concludes.

LOSING THE ANTIBIOTIC MIRACLE

THE 83-YEAR BATTLE between bacteria and the drugs created to kill them falls somewhere between a carnival game of Whack-a-Mole and a nuclear strategy of Mutually Assured Destruction. For almost every antibiotic developed to date, bacteria have evolved a resistance factor that protects them from the drug's attack. For almost every resistance factor, pharmaceutical companies have produced a tougher drug—until now.

Over the decades the battle has gradually tilted to the side of the organisms, like a seesaw slowly shifting out of balance. Bacteria, after all, have evolution on their side. It takes them 20 minutes to produce a new generation. It takes a decade or more to research and develop a new drug. Furthermore, any use—even reasonable use—of antibiotics drives the emergence of resistance by exerting what is known as selective pressure. Typically a few bacteria with random fortunate mutations survive an antibiotic's attack. They reproduce, filling in the living space that the antibiotic cleared for them by killing their susceptible brethren and passing on the genes that protected them. (That is why it is so important to take a full course of antibiotics: to kill all the bacteria causing an infection, not just the most susceptible ones.) But resistance does not spread only via inheritance. By exchanging pieces of DNA, bacteria can acquire resistance without ever having been exposed to the drug the genes protect against.

You can see that pattern of resistance trumping drug trumping resistance in the evolution of *Staphylococcus aureus,* a gram-positive (single-membrane) organism: indifferent first to penicillin, then the synthetic penicillins—including methicillin, earning it the name MRSA—then the cephalosporins such as Keflex, and then vancomycin, the last line of defense against MRSA. Gram-negatives followed a similar pattern, disabling penicillins, cephalosporins, macrolides (erythromycin and azithromycin, or Zithromax) and lincosamides (clindamycin). But until very recently, the carbapenems could safely and reliably dispatch even the most persistent infections, making them the last resort for gram-negative bacteria, the final barrier between treatable and nontreatable infections. They were inexpensive, dependable, broad-spectrum—meaning they worked against many organisms—and very, very strong.

With no new medications in the pipeline capable of dispatching these latest superbugs, we may have to live with the risk of untreatable infections for an uncomfortably long time.

We might be able to research our way out of this dilemma with yet another new class of antibiotics—at least until the bacteria catch up once again. But with no new medications in the 10-year pipeline capable of dispatching these latest superbugs, we may have to live with the risk of many kinds of untreatable infections for an uncomfortably long time.

"It has been hard to discover new compounds that work against gram-negatives and are not toxic to people," says David Shlaes, a physician and drug-development consultant and author of *Antibiotics: The Perfect Storm* (Springer, 2010). "When you think about it, what you are trying to do with an antibiotic is trying to kill something within us, without hurting us. It is challenging." The last new antibiotic licensed for gram-negative infections was doripenem, a carbapenem that was approved by the Food and Drug Administration in 2007.

The situation would be grave enough if it were limited to the few hundred cases that feature the NDM-1 gene so far. But for the past five years another gene conferring similar resistance—dubbed KPC for *Klebsiella pneumoniae* carbapenemase—has moved swiftly across the globe. And it appears to be following the pattern set in the 1950s by penicillin-resistant organisms and in the 1990s by MRSA: first sparking epidemics among vulnerable hospital patients and then spreading into the community at large.

UNCOVERING A HIDDEN THREAT

WHEN WALSH AND GISKE published their NDM-1 results in *Lancet Infectious Diseases* last summer, their paper sparked an immediate international furor. Indian health officials cried foul, charging that the Western doctors were enviously trying to undermine the subcontinent's booming medical-tourism industry.

The first sighting of KPC provoked none of that uproar. It arrived quietly, in one of hundreds of bacterial samples collected during 1996 from hospitals in 18 U.S. states. The project that

Global Threat

For four years after the KPC gene was first isolated from an unidentified hospital in North Carolina, no one could find any evidence of its spread. But once the KPC-bearing bacteria gave rise to outbreaks in several New York City hospitals, the assault was on. The tough-to-kill germs quickly traveled to France, Colombia, Canada, Greece and China. An outbreak in Israel spread to England, Norway and several other European countries.

requested them, called ICARE, was a joint effort of the Atlanta-based Centers for Disease Control and Prevention and Emory University next door. (ICARE stands for Project Intensive Care Antimicrobial Resistance Epidemiology.) The program's goal was to monitor how antibiotics were being used in intensive care units and other hospital departments, in hopes of gauging where the next resistant organism might emerge.

One isolate, sent from a North Carolina hospital that has never been publicly identified, turned out to be *Klebsiella*. That was not unusual. It is a common hospital infection, an almost unavoidable consequence of its use as a treatment in intensive care: high doses of broad-spectrum antibiotics disrupt the ecology of the intestinal tract and cause diarrhea, which contaminates the environment around patients and the hands of the health care workers who treat them. "If you think of a patient in an ICU, sedated, on a ventilator, they can't get up and go to a bathroom," says Arjun Srinivasan, the CDC's associate director for health care–associated infection-prevention programs. "If they are incontinent, the health care staff will have to clean them up. There is lots of equipment close to the patient, and there are lots of surfaces that could become contaminated."

If becoming infected with *Klebsiella* in an ICU was not a surprise, the results of its analysis were. As expected, the North Carolina isolate was resistant to a laundry list of antibiotics, including penicillin and some other related drugs. But the sample was also resistant to two carbapenems—imipenem and meropenem—to which *Klebsiella* had always responded. The sample was not completely resistant, but test results at the CDC indicated that unusually high doses of carbapenems would be needed to treat any infection that it caused. The enzyme that provided that resistance attacked the carbapenem drugs before they could even cross the inner membrane of the bacterial wall.

No one had ever seen a resistance pattern like KPC before. It made the epidemiologists working it up uneasy—as though they were sensing, just at the edge of their hearing, the ring of a distant alarm. "It was a new kind of resistance, but when there is just a single isolate, you don't know how common it is going to be," says Jean B. Patel, deputy director of the CDC's office of antimicrobial resistance. "And for a long time, there were no other isolates like it."

OUTBREAK IN NEW YORK

FOR SEVERAL YEARS the North Carolina *Klebsiella* sample remained a worrisome fluke. Then, in mid-2000, patients in four intensive care units at Tisch Hospital, part of New York University's Langone Medical Center on the east side of Manhattan, began developing unusually tough *Klebsiella* infections that were resistant to almost all the drug classes that an intensive care physician would want to use. It was the first time physicians at N.Y.U. had ever seen infections resistant to carbapenems. Fourteen patients developed highly drug-resistant pneumonia, surgical infections and bloodstream infections, and another 10 were carrying the KPC bug without symptoms. Eight of the 24 died. On analysis, the hospital discovered that their *Klebsiella* strain carried the same key KPC gene as the original North Carolina sample.

The hospital would also soon learn how hard containing the resistant microbe could be. With so many drugs found to be ineffective, the only option was to enforce the old-fashioned tool of rigorous cleanliness, to make sure the resistant bacterium did not travel further on the hands of unknowing health care workers. Langone Medical Center put infected patients into isolation, required anyone going into their rooms to wear gowns and gloves and policed hand-washing and hand-sanitizer use. When those were not enough, they changed the cleaning

Illustration by George Retseck

Exacting Protocol

Health care workers are often unwitting carriers of bacterial resistance. Hospitals that have controlled outbreaks of carbapenem-resistant infection were forced to adopt rigorous hygiene and surveillance measures.

Identify
To avoid missing any potential cases, hospitals in France use rectal swabs to test incoming patients with a history of previous multidrug-resistant infection.

Sterilize
Doctors and nurses must routinely wash hands and wear gloves. Patients are wiped down with antiseptics every day. All surfaces in their room are sanitized, including any computer keyboards.

Review
Laboratory specimens are continually tested and infection-control measures adjusted until multidrug-resistant germs are eliminated.

solutions used in the intensive care units. When infections still rebounded, they zoomed in on the care of the infected patients and discovered that some of them with urinary tract infections were getting splashed when their urine-collection bags were changed—splashes that contaminated the health care workers and the environment as well. It took a year to bring the outbreak under control.

Two years later the same highly resistant bug somehow appeared in hospitals in Brooklyn, further reinforcing how difficult it can be to contain *Klebsiella* harboring the KPC gene. One hospital found two infected patients in August 2003, put them in isolation, immediately ramped up its infection-control practices, and yet by the end of February 2004, 30 more diagnosed cases were scattered through the hospital. Another identified one patient in December 2003 and found two more in February 2004 and 24 additional patients by the end of May, all of them infected in-house despite aggressive efforts to block the microbe's spread.

KPC-bearing bacteria showed up in Harlem Hospital, where they caused an outbreak of seven bloodstream infections in spring 2005; only two patients survived. They also surfaced at Mount Sinai Medical Center on the Upper East Side, where researchers began testing all the patients admitted to three ICUs in hopes of getting a handle on the rapidly spreading epidemic. What they found helped to explain why the bacteria were becoming such a problem: 2 percent of all of the ICU patients were carrying the resistant strain—not showing symptoms but posing a risk of infection to others.

New York City hospitals had become a breeding ground for the resistant germs, something that federal numbers confirmed. In 2007 21 percent of *Klebsiella* samples collected in New York City carried the KPC gene, compared with 5 percent in the rest of the country. In 2008 one New York hospital reported its KPC rate had risen to 38 percent.

Patients in ICUs are seriously ill by definition—they suffer from trauma, cancer, failure of major organs—so their deaths can be complex to sort out, with no single cause. But in certain cases involving KPC, there is no question as to the cause, says John Quale, an associate professor of medicine at S.U.N.Y./Downstate Medical Center in Brooklyn who treated some of the earliest cases in New York. "Clearly, there have been instances where treatment has failed despite every effort," he says. "And patients have died."

GLOBAL SPREAD

FROM NEW YORK CITY, KPC *Klebsiella* spread. It was found first in places that New Yorkers frequently travel to and from—New Jersey, Arizona and Florida—and then much farther away.

Carbapenem resistance is not a reportable disease, meaning that a clinical laboratory that detects its presence is not required to notify public health authorities. So the full extent of the KPC gene's distribution is not known. In 2009, however, half of Chicago hospitals had discovered the KPC gene in at least some of their patients. A year later the proportion of Chicago hospitals reporting the presence of KPC had gone up to 65 percent. By the end of 2010 KPC bacteria had gravely sickened hospital patients in 37 U.S. states. Once the CDC began tracking the bug, officials discovered that hospitals were not prepared for its arrival. "We saw over and over again that an isolate sent to us would end up not being the first in a hospital," says the CDC's Patel. "When they looked back in their data, they would find earlier ones that just had not sparked anybody's attention."

In February 2005 an 80-year-old man who had been living for five years with prostate cancer sought emergency treatment near where he lived in Paris. After he was admitted, doctors found he had brought *Klebsiella* bearing KPC into the hospital, probably from an operation in New York City a few months before. It was the first known move of KPC from the U.S. to another country, but not the last. Soon KPC organisms from New York were found in patients in Colombia, Canada, China and Greece. They caused a 45-person outbreak in a Tel Aviv hospital that traveled via patients and health care workers to England, Norway, Sweden, Poland, Finland, Brazil and Italy.

WHAT NEXT?

HEALTH AUTHORITIES now view the global dissemination of carbapenem resistance—from KPC, NDM-1 and other genes—as a "public health event of international concern," as the World Health Organization put it last November. (The international agency has named "antimicrobial resistance and its global spread" the theme of its annual World Health Day on April 7.) That declaration is in part because so little can be done to stop carbapenem-resistant organisms: only a few antibiotics still work against them, and the drugs are far from perfect.

Most of these infections still respond to tigecycline, a newer drug, and colistin, the decades-old one. Tigecycline, released in 2005, was the first of a new antibiotics class called glycylcyclines; because bacteria had never experienced its mechanism of action before, they have been slow to develop resistance to it. But tigecycline does not diffuse well through the blood or in the

HELEN KING *Corbis*

bladder, rendering it ineffective for bloodstream and urinary tract infections caused by KPC and NDM-1. (Plus, the FDA last year updated tigecycline's label, adding a warning that some patients with severe infections face an unexplained increased risk of death.) Colistin, on the other hand, is one of a small class of drugs called polymyxins that dates back to the 1940s. It has its own issues: in addition to its long-standing reputation for damaging the kidneys, it does not penetrate well into tissues. Those problems kept it from being widely used for decades, and that may be what preserved its usefulness this long—as colistin use has increased in recent years, resistance to it has increased as well.

Beyond tigecycline and colistin, we have almost nothing. Between 1998 and 2008 the FDA approved 13 new antibiotics. Only three had new mechanisms of action, something to which bacteria do not already possess resistance. In 2009 the Infectious Diseases Society of America counted up research efforts on new antibiotics. Out of the hundreds of new drug applications submitted every year to the FDA, they found only 16 antibiotics at any stage of development. Eight of them were intended to treat gram-negative bacteria, but the number that could be used against highly resistant gram-negatives such as KPC and NDM-1 bacteria was zero.

Those statistics make the case: without explicitly saying so, most of the pharmaceutical industry has decided that drugs to treat carbapenem-resistant infections are so challenging to develop and can be used for so short a period before resistance arises, that they are not worth research and development time. "We are getting to the stage now where we need to seriously start investing rather a lot of money into novel compounds—something that we haven't seen before and, more important, that the bacteria haven't seen before," Walsh says. "And we don't need just one or two. We need 10 or 20."

The expanding epidemic has forced hospitals to reassess the efficacy of their infection-control measures. Institutions that have been able to curb the bacteria say that the effort requires ferocious focus. Their protocols include washing down patients with antiseptics every day and cleaning the surfaces in patients' rooms, down to the smallest joints and nooks on monitors and computers, as frequently as every 12 hours. "I worry about disinfection of surfaces. It is where hospitals typically fall down," says Michael Phillips, who is head of infection control at the Langone Medical Center, site of the sentinel outbreak in New York. Phillips helped to develop a novel "Clean Team" project that pairs infection-control experts with the hospital's building-service workers; the team cut the occurrence of several health care infections in its first six months.

LEARN MORE ABOUT DRUG RESISTANCE
ScientificAmerican.com/apr2011/resistance

The newest KPC reports show just how obsessive health workers must be about cleanliness. Last year 28 patients in two French hospitals were infected with resistant *Klebsiella* by endoscopes, flexible fiber-optic viewers that are threaded down the throat and into the digestive tract. The hospitals thought they had sterilized their equipment, but KPC slipped through.

Health care teams are also boosting surveillance, hoping to identify patients who are carriers so they can be isolated before they infect others. France, for instance, has instituted mandatory testing using rectal swabs of all hospital patients who were hospitalized in other countries for a multidrug-resistant infection on the first day of their subsequent admission at a French hospital. "In my own hospital, we had a transfer from Morocco of a patient who was a carrier" of carbapenem resistance, says Patrice Nordmann, chief of the departments of bacteriology and virology at the Bicêtre Hospital in Paris, who treated the first French KPC case in 2005. "We isolated the patient; we rang the alarm. We avoided an outbreak."

In 2009 the CDC published extensive guidelines to help hospitals control carbapenem-resistant bacteria. The agency did not recommend the French strategy of testing every patient before admitting them to the hospital, however, saying the bacteria are still too unevenly distributed across the country to justify the cost and staff time.

Keeping carbapenem-resistant organisms out of hospitals is important not only for controlling outbreaks among debilitated patients. It is also vital for preventing spread to health care workers. Quale and others who documented KPC's movement through New York speculate that some of it may have been unknowingly transported by physicians, nurses and midlevel staff who held jobs in several institutions. And it is even more important for keeping KPC-bearing bacteria from sharing their resistance genes with other bacterial species, such as *E. coli,* that are present in the hospital but also flourish outside it. Such a KPC-fortifed *E. coli* could escape the hospital, passing out of reach of any surveillance scheme.

In at least one case, that escape has happened. In 2008 Israeli physicians treated an elderly man who came into their hospital very sick but with no sign of carbapenem resistance. In his first week in the hospital, he became infected with KPC bacteria. Within a month the KPC gene moved from the *Klebsiella* infection to an *E. coli* residing in the man's own intestines, creating a strain that was very resistant but did still respond to high doses of antibiotics. That transfer of genes happened in the hospital, under the evolutionary pressure of the drugs the man was receiving. But in January of this year researchers in Hong Kong reported that it was happening in the outside world as well. A patient who came to a local outpatient clinic there was revealed to be silently carrying *E. coli* that had acquired NDM-1. There was no record of the man ever having been hospitalized.

Looking ahead, researchers envision the emergence of completely resistant strains of gram-negative bacteria, arriving long before the drugs that could treat them. Some do not have to imagine that happening; they have seen it come true. Three years ago doctors at St. Vincent's Hospital in Manhattan treated two cases of *Klebsiella* that were resistant to everything in their arsenal. One patient survived. One died. "It is a rarity for a physician in the developed world to have a patient die of an overwhelming infection for which there are no therapeutic options," they wrote in a medical journal. "We had no effective treatment to offer." Unless bacterial evolution slows or drug development accelerates, such cases may soon become far too commonplace. SA

MORE TO EXPLORE

Carbapenem-Resistant Enterobacteriaceae: A Potential Threat. M. J. Schwaber and Y. Carmeli in *Journal of the American Medical Association,* Vol. 300, No. 24, pages 2911–2913; December 24, 2008.

The Spread of *Klebsiella pneumoniae* Carbapenemases: A Tale of Strains, Plasmids, and Transposons. L. S. Munoz-Price and J. P. Quinn in *Clinical Infectious Diseases,* Vol. 49, No. 11, pages 1736–1738; December 1, 2009. http://cid.oxfordjournals.org

Does Broad-Spectrum Beta-Lactam Resistance Due to NDM-1 Herald the End of the Antibiotic Era for Treatment of Infections Caused by Gram-Negative Bacteria? P. Nordmann et al. in *Journal of Antimicrobial Therapy.* Published online January 28, 2011.

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IMAGING

NEUROSCIENCE IN THE COURTROOM

Brain scans and other types of neurological evidence are rarely a factor in trials today. Someday, however, they could transform judicial views of personal credibility and responsibility

By Michael S. Gazzaniga

IN BRIEF

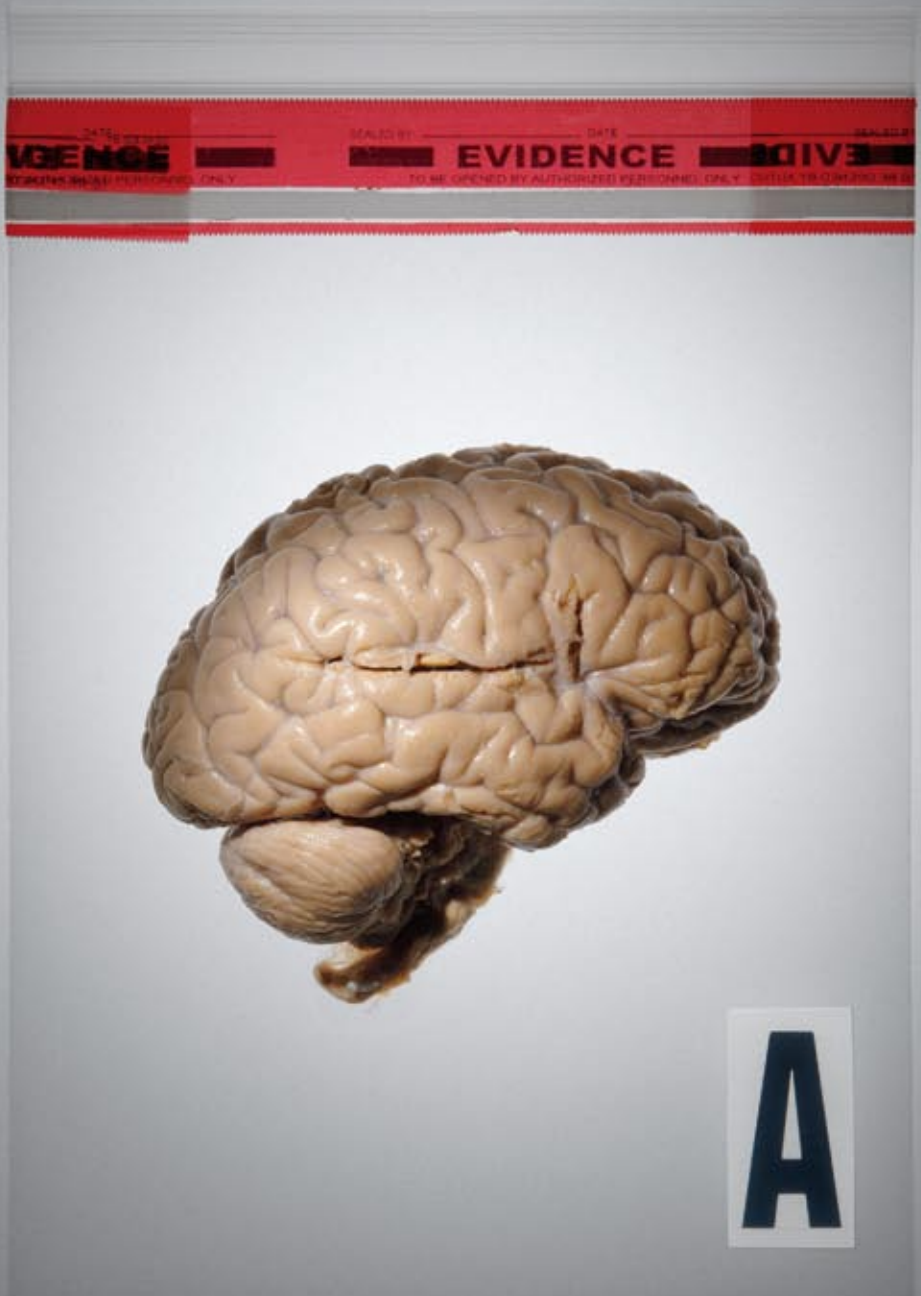
Today courts rarely admit brain scans as evidence at trial for both legalistic and scientific reasons. As neuroscience matures, however, judges may increasingly see such scans as relevant to arguments about a defendant's mental state or a witness's credibility.

The greatest influence of brain science on the law may eventually come from deeper understanding of the neurological causes of antisocial, illegal behaviors. Future discoveries could lay the foundation for new types of criminal defenses, for example.

Yet neurological insights might also upend traditional ideas about personal responsibility and just punishments. The courts—and the rest of society—should therefore proceed with caution in their adoption of findings from neuroscience.

BRAIN COURTESY OF DEPARTMENT OF PATHOLOGY, COLUMBIA UNIVERSITY MEDICAL CENTER

Photograph by Zachary Zavislak



By a strange coincidence, I was called to jury duty for my very first time shortly after I started as director of a new MacArthur Foundation project exploring the issues that neuroscience raises for the criminal justice system. Eighty of us showed up for selection in a case that involved a young woman charged with driving under the influence, but most of my fellow citizens were excused for various reasons, primarily their own DUI experiences. Finally, I was called to the judge. "Tell me what you do," he said.

"I am a neuroscientist," I answered, "and I have actually done work relevant to what goes on in a courtroom. For example, I have studied how false memories form, the nature of addiction, and how the brain regulates behavior."

The judge looked at me carefully and asked, "Do you think you could suspend all that you know about such matters for the course of this trial?" I said I could try. And with that, he said I was excused.

I was dismayed but should not have been. In the interest of fairness, judges and attorneys are supposed to seek jurors who will be guided solely by what they hear in the courtroom and to steer clear of those whose real or imagined outside expertise might unduly influence fellow jurors. Yet, in a way, the judge's dismissal of me also paralleled the legal system's wariness today of the tools and insights of neuroscience. Aided by sophisticated imaging techniques, neuroscientists can now peer into the living brain and are beginning to tease out patterns of brain activity that underlie behaviors or ways of thinking. Already attorneys are attempting to use brain scans as evidence in trials, and the courts are grappling with how to decide when such scans should be admissible. Down the road, an ability to link patterns of brain activity with mental states could upend old rules for deciding whether a defendant had control over his or her actions and gauging to what extent that defendant should be punished. No one yet has a clear idea of how to guide the changes, but the legal system, the public and neuroscientists need to understand the issues to ensure that our society remains a just one, even as new insights rock old ideas of human nature.

The use of neuroscience to assess the character and overall honesty of defendants may eventually trump its use for probing their truthfulness on any one matter.

UNACCEPTABLE EVIDENCE (FOR NOW)

With the growing availability of images that can describe the state of someone's brain, attorneys are increasingly asking judges to admit these scans into evidence, to demonstrate, say, that a defendant is not guilty by reason of insanity or that a witness is telling the truth. Judges might approve the request if they think the jury will consider the scans as one piece of data supporting an attorney's or a witness's assertion or if they think that seeing the images will give jurors a better understanding of some relevant issue. But judges will reject the request if they conclude that the scans will be too persuasive for the wrong reasons or will be given too much weight simply because they look so impressively scientific. In legal terms, judges need to decide whether the use of the scans will be "probative" (tending to support a proposition) or, alternatively, "prejudicial" (tending to favor preconceived ideas) and likely to confuse or mislead the jury. So far judges—in agreement with the conventional wisdom of most neuroscientists and legal scholars—have usually decided that brain scans will unfairly prejudice juries and provide little or no probative value.

Judges also routinely exclude brain scans on the grounds that the science does not support their use as evidence of any condition other than physical brain injury. Criminal defense attorneys may wish to introduce the scans to establish that defendants have a particular cognitive or emotional disorder (such as flawed judgment, morality or impulse control), but—for now at least—most judges and researchers agree that science is not yet advanced enough to allow those uses.

Functional magnetic resonance imaging (fMRI) offers an example of a process that can provide good scientific information, of which fairly little is legally admissible. This technology is a favorite of researchers who explore which parts of the brain are active during different processes, such as reading, speaking or daydreaming. It does not, however, measure the firing of brain cells directly; it measures blood flow, which is thought to correlate to some extent with neuronal activity. Further, to define the imaging signal associated with a particular pattern of brain activity, researchers must usually average many scans from a group of test subjects, whose individual brain patterns may diverge widely. A defendant's fMRI scan may appear to differ greatly from an average value presented in court but could still be within the statistical boundaries of the data set that defined that average.

Moreover, scientists simply do not always know the prevalence of normal variations in brain anatomy and activity in the population (or groups within it). Showing a defendant's brain scan without data from an appropriate comparison group might profoundly mislead a jury. Judges have already had a hard time evaluating whether to admit physical brain-scan evidence of neurological or psychiatric problems that might bear on a defendant's culpability; they may face more difficulty in the years ahead when deciding whether to allow brain images to serve as indicators for more complex mental states, such as a witness's credibility or truthfulness.

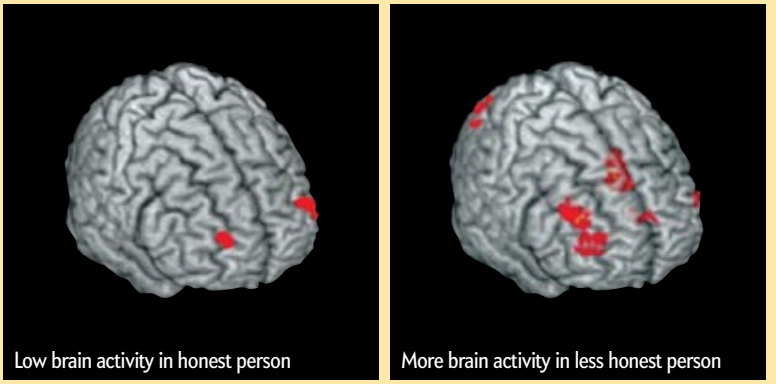
Since the early 20th century, when psychologist and inventor William Moulton Marston first claimed that a polygraph measuring blood pressure, pulse, skin conductivity and other physiological signs could determine whether someone is lying, lie detection has been a hot topic in legal circles. U.S. courts have largely dismissed polygraph results as inadmissible, but other technologies are being developed, and courts will surely be forced eventually to evaluate their admissibility as well. These tools include brain-imaging methods that aim to detect mental states reflective of truthful behavior.

DETECTING LIES AND DETERMINING CREDIBILITY

Recent work by Anthony D. Wagner and his colleagues at Stanford University, for instance, has revealed that under controlled experimental conditions fMRI, combined with complex analyti-

A Neurological Struggle with Temptation

An intriguing study demonstrates one pitfall of using brain scans as lie detectors in the courtroom. Functional magnetic resonance imaging scans taken during tests of subjects' honesty found that compared with consistently truthful people (*left*), those who sometimes lied (*right*) exhibited more neural activity (*red*) in brain areas involved in cognitive control. The extra activity was present whether or not the subjects behaved dishonestly in a particular instance. Consequently, such activity does not reveal whether someone is lying. It only suggests that he or she is using cognitive control when confronted with an opportunity to lie.



cal algorithms called pattern classifiers, can accurately determine that a person is remembering something but not whether the content of the detected memory is real or imagined. In other words, we might be able to use fMRI to detect whether individuals believe that they are recalling something, but we cannot tell whether their beliefs are accurate. Wagner concludes that fMRI methods may eventually be effective in detecting lies but that additional studies are needed.

Other experiments help to expose the nature of honesty: Does honesty result from the absence of temptation or from the exercise of extra willpower to resist it? In 2009 Joshua D. Greene and Joseph M. Paxton of Harvard University gave test subjects placed in a scanner a financial incentive to overstate their accuracy in a coin toss; the researchers were able to obtain fMRI images of individuals deciding whether or not to lie. Dishonest behavior correlated with extra activity in certain brain regions involved in impulse control and decision making. Yet Greene and Paxton noted that some subjects who told the truth also exhibited that same brain activity, so the fMRI images may capture only their extra struggle to resist temptation, not their ultimate truthfulness. The researchers therefore urge judges to be cautious about allowing these kinds of data in today's courtroom.

Their view is not universal, however. Frederick Schauer, professor of law at the University of Virginia and an expert on legal evidence, points out that courts now routinely admit many types of evidence that are far more dubious than the lie-detection science that is being excluded. The current approach to assessing whether witnesses or others are telling the truth is inaccurate and based on misconceptions about dishonest behavior: demeanor, for example, does not always provide reliable clues to honesty. The law has its own standards for determining admissibility into a court, and those standards are more lenient than scientific standards. Schauer argues that jurors should be allowed to consider the result of a lie-detection test that has a 60 percent accuracy rate because it could provide reasonable doubt as to guilt or innocence.

One of the first cases to tackle the use of brain-scanning technology for lie detection recently ended in a federal district court in Tennessee. In *United States v. Semrau,* a magistrate judge found that the evidence offered by a commercial fMRI lie-detection company should be excluded in part because of Federal Rule of Evidence 403, which holds that evidence must be probative and not prejudicial.

Furthermore, the judge explained why he found that the unfair prejudicial influence of the technology in the case substantially outweighed its probative value. The magistrate's main objection was that the defense expert conducting the lie-detection test could not tell the court whether the answer to any particular question was true or false. In fact, the expert testified that he could tell only whether the defendant was answering the set of questions about the case truthfully overall.

One must wonder: In future cases, might the results be admissible with the more limited goal of simply determining whether or not the defendant was being deceptive in general? The use of neuroscience to assess the character and overall honesty of defendants may eventually trump its use for probing their truthfulness on any one matter in the courtroom. Federal Rule 608(b) provides that once the character of a witness has been attacked, counsel can introduce as evidence opinions about the witness's "character for truthfulness or untruthfulness." Today this type of evidence consists simply of testimony by others about the character of the witness. But what about tomorrow? Will juries want to know how a witness scores on a test of probable dishonesty? Will the evidence that someone tends toward dishonesty be more prejudicial if it comes out of a fancy machine? My guess is that such evidence will eventually be used and that it will initially tend to be prejudicial but that as society acquires more experience with the technology, the prejudicial effect will diminish.

SCANNING FOR PSYCHOPATHS

JUDGES AND ATTORNEYS are already being forced to work out the role of brain scans in the courtroom. In the long run, however, the greatest impact of neuroscience on the legal system will surely come from deeper insights into how our brain shapes our behavior. Even in infancy humans manifest innate senses of fairness and reciprocity, as well as desires to comfort the mistreated and punish transgressors. We are judge and jury from birth. On top of these instincts we have built our enlightened view of how culture should regard and punish antisocial behavior. Someday neuroscience could well force the legal system to revise its rules

FROM "PATTERNS OF NEURAL ACTIVITY ASSOCIATED WITH HONEST AND DISHONEST MORAL DECISIONS," BY JOSHUA D. GREENE AND JOSEPH M. PAXTON, IN *PNAS*, VOL. 106, NO. 30; JULY 28, 2009

for determining culpability and for meting out sentences. It could also shake up society's understanding of what it means to have "free will" and how best to decide when to hold someone accountable for antisocial actions.

Consider the psychiatric and legal standing of psychopaths, who constitute less than 1 percent of the general population but roughly 25 percent of those in prison. That label, though used popularly as a catchall for many violent and nonviolent criminals, is properly reserved for those with a well-defined psychiatric condition diagnosed through a test called the Hare Psychopathy Checklist-Revised (PCL-R).

Psychopaths often display superficial charm, egocentricity, grandiosity, deceitfulness, manipulativeness, and an absence of guilt or empathy, all of which the PCL-R can assess. Yet psychometric tests such as the PCL-R are only proxies for measuring the neurological dysfunctions underlying these people's disturbed mental lives. Neuroimaging measurements of brain processes should therefore, at least in theory, provide a much better way to identify psychopaths.

To date, numerous studies have associated psychopathy with unusual brain activity. Psychopaths seem to exhibit, for example, abnormal neurological responses to stimuli that demand close attention and to words with emotional, concrete or abstract meanings. But such responses may also be found in people who have suffered damage to an area known as the medial temporal lobe—meaning they cannot be used as definitive signs of psychopathy. Other studies suggest psychopaths may have damage to the deep-brain structures of the limbic system, which helps to give rise to emotions, but the finding is preliminary.

Scientists are also beginning to look for abnormal connections in psychopaths' brains. Marcus E. Raichle, Benjamin Shannon and their colleagues at Washington University in St. Louis, along with Kent Kiehl of the University of New Mexico, analyzed fMRI data from scans of adult inmates and of juvenile offenders, all of whom were also assessed for psychopathy with the PCL-R. The adults, they found, had a variety of unusual connections between regions in their brains, although no one alteration predominated. Striking differences appeared more consistently and exclusively in the young offenders—and the degree of those changes increased along with their individual levels of impulsivity. One interpretation is that the impulsive juveniles lack some of the normal neural constraints on their choices of actions. Perhaps among juveniles who go untreated a brain abnormality that promotes impulsiveness eventually becomes more widespread, resulting in the diverse neural abnormalities seen in adults. Such a difference may also help explain why psychiatric treatments for psychopathy in juveniles are more successful than in adults, who are largely unresponsive.

Controversially, psychopathy is not now a recognized basis for an insanity defense. Instead psychopaths are seen as more dangerous than offenders without the pathology, and they receive longer or harsher sentences. A neuroimaging tool or method that could reliably identify psychopaths would be useful at the sentencing phase of a trial because it could help determine whether the defendant might deserve medical confinement and treatment rather than punitive incarceration. Getting the public to accept that people identified in this way should be committed to a mental hospital instead of a prison may be a tough sell, but with enough evidence the practice could eventually become legal doctrine. By then, one hopes, neuroscience will also have come up with better ways to help rehabilitate or cure them.

NEUROSCIENCE AND CRIMINAL DEFENSES

CRIMINAL LAW currently accepts only a short list of possible defenses—will modern neuroscience begin to add to it? For example, the courts have consistently refused to accept a formal "battered woman defense" from defendants who retaliated with lethal force against spouses who regularly and violently beat them. Nevertheless, in some states the courts do allow experts to testify that battered-woman syndrome is a type of post-traumatic stress disorder, which judges and juries can take into consideration when assessing the credibility of a woman's claim that she acted to protect herself. Such precedents open a door to wider judicial uses of neuroscience.

How one defines a defendant's *mens rea,* or mental state, in a

PROCEDURES

Before Brain Scans Can Be Evidence

Like all forms of scientific evidence, brain scans must pass through at least two stages of review and sometimes more before juries are allowed to hear them. Attorneys can appeal a decision about the admission of the brain scans as evidence only if the judge seems to have abused his or her discretion in a case.

By the Defense

Defense attorney hires an expert to conduct a neurological review of a client or witness and render an opinion. If the opinion is unhelpful to the client's case, the attorney does not disclose it.

By the Judge

At a pretrial hearing, a judge determines whether any submitted brain scans meet the statutory requirements for evidence and whether their informative value exceeds their potential to prejudice a verdict.

At the Trial

If a case goes to trial (which can be relatively rare), attorneys can present brain scans approved by the judge to a jury for consideration in its verdict.

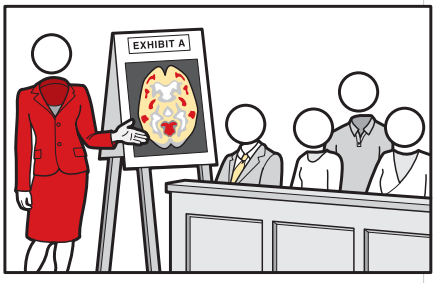


Illustration by Brown Bird Design

given context has a major effect on how much responsibility to ascribe to him or her. In ongoing fMRI-based research, Read Montague of Baylor College of Medicine and Gideon Yaffe, a law professor at the University of Southern California, study whether certain addicted individuals suffer from a subtle form of "risk blindness." Reasonable people learn not to rob stores by realizing that committing the crime would jeopardize their ability to enjoy a life with friends and family, pursue rewarding careers, and so on. Montague and Yaffe see indications, however, that at least some addicts cannot think through the benefits of those alternative courses of action. Potentially their findings could justify modifying the "reasonable person" standard in criminal law so addicts could be judged against what a reasonable addict, rather than a reasonable nonaddict, would have done in a given situation; such a finding might then lead to acquittal or reduction in punishment for an addicted defendant.

Would it erode notions of free will and personal responsibility if all antisocial decisions could seemingly be attributed to some kind of neurological deviations?

AUTHOR INTERVIEW AND MORE
ScientificAmerican.com/apr2011/gazzaniga

When the foregoing examples are taken together, profound questions emerge about how our culture and the courts will manage antisocial behavior. As neuroscientist William T. Newsome of Stanford University has asked, Will each of us have a personalized "responsibility" ranking that may be called on should we break the law? If we soon all carry our personal medical histories on a memory stick for reference, as some experts predict, will we also perhaps include a profile derived from knowledge of our brain and behavior that captures our reasonableness and irresponsibility? Would this development be good for society and advance justice, or would it be counterproductive? Would it erode notions of free will and personal responsibility more broadly if all antisocial decisions could seemingly be attributed to some kind of neurological deviations?

I feel it is important to keep scientific advances on how the brain enables mind separate from discussions of personal responsibility. People, not brains, commit crimes. As I have spelled out elsewhere, the concept of personal responsibility is something that arises out of social interactions. It is a part of the rules of social exchange, not a part of the brain.

PROCEED WITH CAUTION

IN SPITE OF THE MANY INSIGHTS pouring forth from neuroscience, recent findings from research into the juvenile mind highlight the need to be cautious when incorporating such science into the law. In 2005 in the case *Roper v. Simmons,* the U.S. Supreme Court held that the execution of a defendant who committed a murder at age 17 or younger was cruel and unusual punishment. It based its opinion on three differences between juveniles and adults: juveniles suffer from an impetuous lack of maturity and responsibility; juveniles are more susceptible to negative influences and lack the independence to remove themselves from bad situations; and a juvenile's character is less formed than an adult's. Although the court realized it was drawing an arbitrary line, it ruled that no person who was younger than 18 at the time of a crime could receive the death penalty.

In May 2010 the court expanded that limitation. In *Graham v. Florida,* it held that for crimes other than homicide, a sentence of life without the possibility of parole for a person under the age of 18 violated the Constitution's prohibition of cruel and unusual punishment. Citing information provided by the American Medical Association, the court stated that "psychology and brain science continue to show fundamental differences between juvenile and adult minds."

But how consistently do neuroscience and psychology support that opinion? A study by Gregory S. Berns, Sara Moore and C. Monica Capra of Emory University explored whether the irrefutable tendency of juveniles to engage in risky behavior resulted from immaturity in the cognitive systems that regulate emotional responses. This team tested the theory using a technology called diffusion tensor imaging (DTI) to examine the tracts of white matter that connect different control regions of the cortex in 91 teenage subjects. Surprisingly, the juveniles who engaged in risky behavior had tracts that looked *more adult* than did those of their more risk-averse peers.

Advanced neuroimaging has thus presented a finding directly contrary to the conventional scientific and legal perspectives on the capacity of juveniles. If further research supports those conclusions, then the law, by its own logic, might need to hold juvenile delinquents to adult criminal standards. Alternatively, justice might require that convicted juveniles undergo DTI or a successor technology to determine whether their white matter structure is adultlike. The results of such a test could then provide guidance to the court on sentencing. The scope of these consequences highlights why the courts should not incorporate insights from neuroscience into the law until a substantial body of studies have confirmed them.

Exciting as the advances that neuroscience is making everyday are, all of us should look with caution at how they may gradually come to be incorporated into our culture. The legal relevance of neuroscientific discoveries is only part of the picture. Might we someday want brain scans of our fiancées, business partners or politicians, even if the results could not stand up in court? As the scientific understanding of human nature continues to evolve, our moral stance on how we wish to manage a just society will shift as well. No one I know wants to rush into a new framework without extreme care being given to each new finding. Yet no one can ignore the changes on the horizon. SA

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The Law and Neuroscience Project: www.lawandneuroscienceproject.org

Eitan Haddok is a Paris-based photographer and reporter who has a master's degree in geophysics and planetary sciences. He created our October 2008 photo feature "Birth of an Ocean."

ENVIRONMENT

Can the Dead Sea Live?

Irrigation and mining are sucking the salt lake dry, but together Israel, Jordan and the Palestinian Authority could save the sacred sea

Story and photographs by Eitan Haddok

THE DEAD SEA IS A PLACE OF MYSTERY: THE LOWEST SURFACE ON EARTH, THE PURported site of Sodom and Gomorrah, a supposed font of curative waters and, despite its name, a treasure trove of unusual microbial life. Yet its future is anything but a mystery. After centuries of stability—owed to a delicate equilibrium between freshwater supply from the Jordan River and evaporation under the relentless Middle Eastern sun—the lake is now disappearing.

Jordanians to the east, Israelis to the west, and Syrians and Lebanese to the north are pumping so much freshwater from the river catchment that almost none reaches the sea. Israel and Jordan are also siphoning water from the lake to extract valuable minerals, hastening the decline. Thousands of sinkholes have formed in the receding sea's wake, curtailing tourism and development along the border because no one can predict where the next gaping hole will suddenly open, potentially swallowing buildings, roads or people.

Concerned over losing a valuable natural and cultural resource, officials from Israel, Jordan and the Palestinian Authority have proposed an enormous conveyor system that would steadily refill the Dead Sea with water from the Red Sea to the south. Scientists are testing how the mixing waters might affect the lake's chemistry and biology or if the influx could turn the lake red. Politicians are testing whether either nation has the will to fund the $10-billion lifeline, as environmentalists oppose the pharaonical project. And governments that preside over other saline bodies, including the Aral Sea, the Caspian Sea and the Great Salt Lake in Utah, are watching for lessons that could apply to their own future development. Take a tour here of the dying sea and efforts to bring it back to life.

IN BRIEF

The Dead Sea, 424 meters below sea level, is dropping by a meter a year as feedwaters are tapped for irrigation and seawater is evaporated for minerals extraction.
Thousands of sinkholes are forming as receding underground saltwater allows the ground above to collapse.
A 180-kilometer system of pipes could supply needed brine from the Red Sea. Scientists are testing how the mixing waters might alter sea life.

The Dead Sea now lies 424 meters below sea level, and the water is dropping by one meter a year. In certain places, the water's edge has receded a full kilometer from shore. More than 3,000 sinkholes have opened around the perimeter—in recent years, about one every two days. Some fill with brine; others do not.

2

3

4

SUNK BY TEMPTATION

SINKHOLES (*1*) can be up to 25 meters wide and 15 meters deep. They can open abruptly, swallowing trekkers as well as buildings and roads (*3*).

Dissolution is the most widely accepted explanation: as salty lake water recedes, underground saltwater recedes along with it. Fresher underground water moves in, contacts salt layers below the surface and dissolves them, causing the surface to collapse.

Some large holes fill with brine; others do not. Lines of sinkholes sometimes form above shallow geologic faults (*2*), which can allow freshwater to intrude as saltwater recedes. Understanding such mechanisms could help explain odd sinkhole formation in Florida, Guatemala, Germany and Spain.

The sea is emptying primarily because influx from the Jordan River to the north has dwindled from about 1,300 million cubic meters a year to 30 million cubic meters a year. As a result, evaporation in the sea outstrips freshwater supply; the southern lobe of the lake has disappeared.

The river loss is caused by pumps in Israel, Jordan, Syria and Lebanon that take water for agriculture or domestic use (*4*); some pipes become defunct as the river is tapped out (*foreground of photograph*).

1

3

COURTESY OF NASA AND USGS (*top left*)

2

4

POSSIBLE RESURRECTION

THE SEA IS ALSO DROPPING because the Dead Sea Works company in Israel and the Arab Potash Company in Jordan pipe water from the north through a canal to the south; there it spills into enormous, artificial, cascading ponds where the southern lobe used to be (*1, blue,* and *2, closer view*). Evaporation leaves behind concentrated minerals such as bromine, magnesium and potash, as well as salts (*3*), all of which the companies extract. Air above the vast pond region contains some of the highest levels of oxidized mercury on earth—formed because of high bromine concentration.

Under current conditions, the Dead Sea could sink to –550 meters by 2200. The retreat could be stopped by 180 kilometers of proposed canals and pipelines that would bring in water from the Red Sea. Desalination plants along the conveyor would produce 900 million cubic meters of freshwater a year, most of which would go to Jordan. The remaining 1.1 million cubic meters of briny water would be injected into the Dead Sea. Hydroelectric plants could exploit the drop in elevation along the way. A $17-million feasibility study by the World Bank should be completed by July. If it is built, the conveyor could stabilize the sea's level at –410 to –420 meters by 2050.

VIEW A SLIDE SHOW
ScientificAmerican.com/apr2011/haddok

Brine from desalination might not be a suitable substitute for Jordan River water. The brine and the sea's saltwater could stratify in layers. Algae and bacteria could grow, perhaps changing the sea's color from turquoise to reddish. Experiments in small tanks conducted by microbiologists suggest algae blooms might indeed occur (*4*), but tests are not yet conclusive or independently duplicated.

Saving the Dead Sea could pay off in various ways. Biologists recently discovered a new form of metabolism in certain microorganisms in the water. Scientists have also transplanted genes from a unique local fungus into a yeast strain that subsequently has shown strong resistance to saline stress, as well as heat and oxidative stress. The gene could potentially help crops grow in saline soils now unsuitable for cultivation, which could bring food security to millions of people in salty lands worldwide. SA

MORE TO EXPLORE

Information about the proposed Red Sea–Dead Sea conveyor can be found at www.foeme.org and www.worldbank.org

Graham P. Collins holds a Ph.D. in physics from Stony Brook University and is a contributing editor to *Scientific American*.

ARTIFICIAL INTELLIGENCE

Solving the Cocktail Party Problem

Computers have great trouble deciphering voices that are speaking simultaneously. That may soon change *By Graham P. Collins*

YOU ARE AT A PARTY, AND ALEX IS TELLING A BORING STORY. YOU are much more interested in the gossip that Sam is recounting to Pat, so you tune out Alex and focus on Sam's words. Congratulations: you have just demonstrated the human ability to solve the "cocktail party problem"—to pick out one thread of speech from the babble of two or more people. Computers so far lack that power.

Although automated speech recognition is increasingly routine, it fails when faced with two people talking at once. Computerized speech separation would not only improve speech-recognition systems, it could also advance many other endeavors that require the separating of signals, such as making sense of brain-scan images.

The problem is devilishly hard. In the past several years, however, computer scientists have made exciting progress. One group has even achieved a very rare feat in automated perception: outperforming humans.

WHY SO DIFFICULT?

Separating two streams of words is far more challenging than understanding the speech of one talker because the number of possible sound combinations is astronomical. Applying the usual techniques of ordinary (single-talker) speech recognition in brute-force fashion, to explore all the alternative ways that multiple talkers might have produced the combined sound, would be far too time-consuming. To solve the cocktail party problem efficiently, then, an algorithm must exploit special characteristics of speech sounds.

Whether one person is talking or many, the sound contains a spectrum of frequencies, and the intensity of each frequency changes on a millisecond timescale; spectrograms display data of this kind. Standard single-talker speech recognition analyzes the data at the level of phonemes, the individual units of sound that make up words—F-OH-N-EE-M-Z. Each spoken phoneme produces a variable but recognizable pattern in the spectrogram.

Statistical models play a major role in all speech recognition, specifying the expected probability that, for instance, an "oh" sound will be followed by an "n." The recognition engine looks for the most likely sequences of phonemes and tries to build up whole words and plausible sentences.

When two people talk at once, the number of possibilities explodes. The frequency spectrum at each moment could come from any two phonemes, enunciated in any of the ways each person might use them in a word. Each additional talker makes the problem exponentially worse.

PROMISING IDEAS

Fortunately, though, sounds of speech tend to be "sparse": a spectrogram of two speakers usually has many a small region in which one

IN BRIEF

Computers cannot yet solve the "cocktail party problem"—understanding speech when two or more people are talking at the same time.

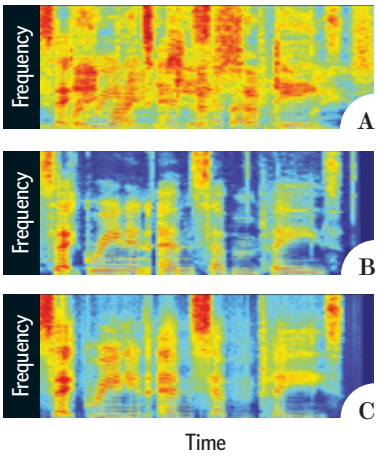
A number of groups are making good progress, though, using various methods.

A multimedia feature, which is available at www.ScientificAmerican.com/apr2011/speech, describes the logic behind one leading approach in detail and allows you to test your own ability to separate overlapping streams of chatter.

Illustration by Bryan Christie

Voice Prints

Spectrograms display the changing levels of sound across a range of frequencies over time—those at the right record speech samples two seconds long. The color scale goes from loud (*red*) to quiet (*blue*). With four people talking simultaneously (A), the stream of sound coming from one of the speakers (B) is hard to discern. A new algorithm for speech separation, however, was able to estimate that person's speech (C) accurately enough for a computer to recognize what the individual said.



speaker is much louder than the other. For those regions, ordinary speech recognition can find prospective phonemes matching the dominant speaker, greatly simplifying the search. It is by exploiting such features as sparseness that computer scientists have made great strides recently in finding shortcuts through the combinatorial jungle of speech separation. They follow two main approaches.

One method works from the bottom up, examining basic features in a spectrogram to discern which regions come from the same talker. For example, a sudden onset of sound at two different frequencies at the same instant probably comes from one talker.

This approach often also looks for spectrogram regions where neither talker dominates. The algorithms then set aside those corrupted regions and try to find phoneme sequences matching the clean regions. A group at the University of Sheffield in England has achieved good results using these methods. In a report published in 2010 comparing how well 10 different algorithms performed on a collection of benchmark overlapping speech samples, the Sheffield group had the third-best overall accuracy.

Most research groups, however, take a top-down, or "model-based," approach. Their algorithms look for sequences of phonemes that are plausible individually and that combine to produce the total sound. Because considering every possible combination of overlapping phonemes is far too inefficient, the trick is to simplify or approximate the process without sacrificing too much accuracy.

Tuomas Virtanen of the Tampere University of Technology in Finland simplified the search by focusing alternately on each of the two talkers. In essence: given the current best estimate of talker A's speech, search for talker B's speech that best explains the total sound. Then keep repeating with the roles reversed every time. The Tampere algorithm edged out the Sheffield group's for the second-highest accuracy, although it remained more than 10 percentage points behind human listeners.

The first-ever demonstration of "superhuman" automated speech separation was achieved by a group at the IBM Thomas J. Watson Research Center in Yorktown Heights, N.Y. This team's latest algorithm works efficiently even when more than two people are talking—it has separated speech streams of four overlapping talkers. In part, the algorithm carries out the usual top-down analysis, evaluating trial sequences of phonemes for all the speakers. Between iterations of this search, the program uses its most promising estimates of the speech to look for spectrogram regions where one talker was loud enough to mask the others. Interestingly, attending to such masking makes it practical to refine the estimate of all the talkers' speech simultaneously.

Automated speech separation still has a long way to go before computers will be able to routinely eavesdrop on gossip at noisy parties. Yet the recent results suggest that prospect may finally be coming into view, if not yet within earshot. SA

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CELL BIOLOGY

the orderly chaos of proteins

To do their magic in the cell, proteins must fold into rigid shapes—or so standard wisdom says. But a more tangled story is beginning to emerge

By A. Keith Dunker and Richard W. Kriwacki

IN BRIEF

According to conventional wisdom, proteins must fold into rigid shapes to perform such tasks as binding to specific target molecules. But recent work suggests that one third of the types that exist in humans are partially or completely unstructured.

Although lack of folding was long considered a pathology, it need not hamper functionality—and it is in fact often crucial to a protein's workings.

Unstructured proteins may have played important roles during evolution, and a better understanding of their true nature may also lead to the design of novel drugs.

PROTEINS ARE THE STUFF OF life. They are the eyes, arms and legs of living cells. Even DNA, the most iconic of all molecules in biology, is important first and foremost because it contains the genes that specify the makeup of proteins. And the cells in our body differ from one another—serving as neurons, white blood cells, smell sensors, and so on—largely because they activate different sets of genes and thus produce different mixtures of proteins.

Given these molecules' importance, one would think biologists would have long figured out the basic picture of what they look like and how they work. Yet for decades scientists embraced a picture that was incomplete. They understood, quite properly, that proteins consist of amino acids linked together like beads on a string. But they were convinced that for a protein to function correctly, its amino acid chain first had to fold into a precise, rigid configuration. Now, however, it is becoming clear that a host of proteins carry out their biological tasks without ever completely folding; others fold only as needed. In fact, perhaps as many as one third of all human proteins are "intrinsically disordered," having at least some unfolded, or disordered, parts.

Illustrations by AXS Biomedical Animation Studio

A. Keith Dunker is a biophysicist at the Indiana University School of Medicine, where he directs the Center for Computational Biology and Bioinformatics. He studied viruses for 30 years before immersing himself in the study of disordered proteins in 1995.

Richard W. Kriwacki is a structural biologist at St. Jude Children's Research Hospital in Memphis. In 1996, while at the Scripps Research Institute in La Jolla, Calif., he co-discovered one of the first examples of a truly unstructured protein.

Folding only as needed, the flexible protein p27 (*green*) can wrap around many different partners, something that proteins with a unique 3-D structure cannot do.

To be sure, biologists have known for a while that enzymes such as the polymerases that copy DNA or transcribe it into RNA are complicated nanomachines consisting of many moving parts, with hinges that allow different segments of a protein to pivot around one another. But those proteins are often pictured as combinations of rigid parts, like the sections of a folding chair. Intrinsically disordered proteins look more like partially cooked spaghetti constantly jiggling in a pot of boiling water.

Fifteen years ago this assertion would have seemed downright heretical. Today scientists are realizing that such amorphous and flexible features probably helped life on earth get started and that their flexibility continues to play critical roles in cells, for instance, during cell division and gene activation. And this new understanding offers more than startling new insights into the basic biology of cells. Equally exciting, it hints at new ways for treating disease, including cancer.

PERFECT MATCHES

THE NOTION that a rigid, three-dimensional structure determines a protein's function first emerged in 1894. Emil Fischer, a chemist at the University of Berlin, proposed that enzymes—the catalysts of biochemical reactions—interact with other molecules by binding to specific shapes on their outer surface; at the same time, enzymes would completely ignore any molecules whose surface features are only slightly different. In other words, an enzyme and its binding partner fit together like a key and a lock.

At the time Fischer formulated his model, the nature of proteins was unknown. Over the next 60 or so years biologists learned that proteins were chains of amino acids and concluded that they had to fold into a precise shape to work properly. In 1931 Chinese biochemist Hsien Wu lent strong support to that view, showing that protein denaturation, or loss of natural 3-D structure, led to a complete loss of function. Since then, starting with the 3-D structure of sperm whale myoglobin in 1958, researchers have determined the architecture of more than 50,000 types of protein, usually by first coaxing their rigid structure into forming crystals and then scattering x-rays off those crystals.

Not all was static in this structured, lock-and-key protein world, though. As far back as the early 1900s, scientists knew that many antibodies can bind to multiple targets, or antigens—an observation that did not fit neatly with the lock-and-key model. In the 1940s the great chemist Linus Pauling speculated that certain antibodies can fold up in any of several ways, with the folding of each configuration guided by the fit between antibody and antigen.

From about the 1940s on, various other observations indicated that not all proteins abided by the dogma that function follows from a rigid, 3-D structure. But those that did not were usually regarded as isolated, freak exceptions to the rule. One of us (Dunker) was among the first researchers to collect such examples and to note that perhaps the dogma itself needed revision. In 1953, for instance, scientists noticed that the milk protein casein is largely unstructured; this pliability probably facilitates its digestion by infant mammals. In the early 1970s a protein called fibrinogen was found to contain a region of significant size having no fixed structure; this region, along with similar but smaller ones discovered later, plays a key role in blood clotting. Later in the 1970s, the protein that forms the outer casing, or capsid, of the tobacco mosaic virus offered another striking example. When the capsid is empty, the protein has large, unstructured regions hanging loose inside the capsid's cavity; that looseness enables newly minted RNA, made during viral reproduction in an infected cell, to pack inside. But as the RNA gets in, the protein binds to it and sets into a rigid shape.

Meanwhile experimenters who could not induce certain proteins to fold in their test tubes assumed they were doing something wrong: surely the amino acid chains would find a "correct" folded shape in the environment of the cell. For example, when researchers placed solutions containing isolated proteins into vials and scanned them with a nuclear magnetic resonance (NMR) spectrometer—a workhorse of protein studies—they would sometimes get blurry data, which they interpreted as indicating that the proteins had failed to fold.

But those data had a richer story to tell. NMR spectroscopy involves the application of powerful radio-frequency pulses to induce the atomic nuclei of particular elements, such as hydrogen, to spin in sync. Slight frequency shifts in the nuclei's response correlate tightly to the atoms' positions inside amino acids and to the positions of those amino acids with respect to one another. Thus, from these frequency shifts investigators can often piece together the structure of a rigid protein. But if the amino acids move a lot—as would be the case in an unfolded protein—the frequency shifts become blurry.

In 1996 one of us (Kriwacki, then at the Scripps Research Institute) was performing NMR spectroscopy on a protein called p21, involved in controlling cell division, when he noticed something shocking. According to his NMR data, p21 was almost entirely disordered. The amino acids freely rotated about the chemical bonds that held them together, never staying in one conformation for more than a fraction of a second. And yet—and this was the shocking part—p21 was still able to perform its critical regulatory function. It was the first convincing demonstration that lack of structure does not make a protein useless.

NMR spectroscopy remains the primary technique to determine whether a protein is folded or disordered, and together with other technologies it has now confirmed that many proteins are intrinsically disordered. These molecules constantly morph under the action of Brownian motion and their own thermal jitters, and yet they are perfectly functional.

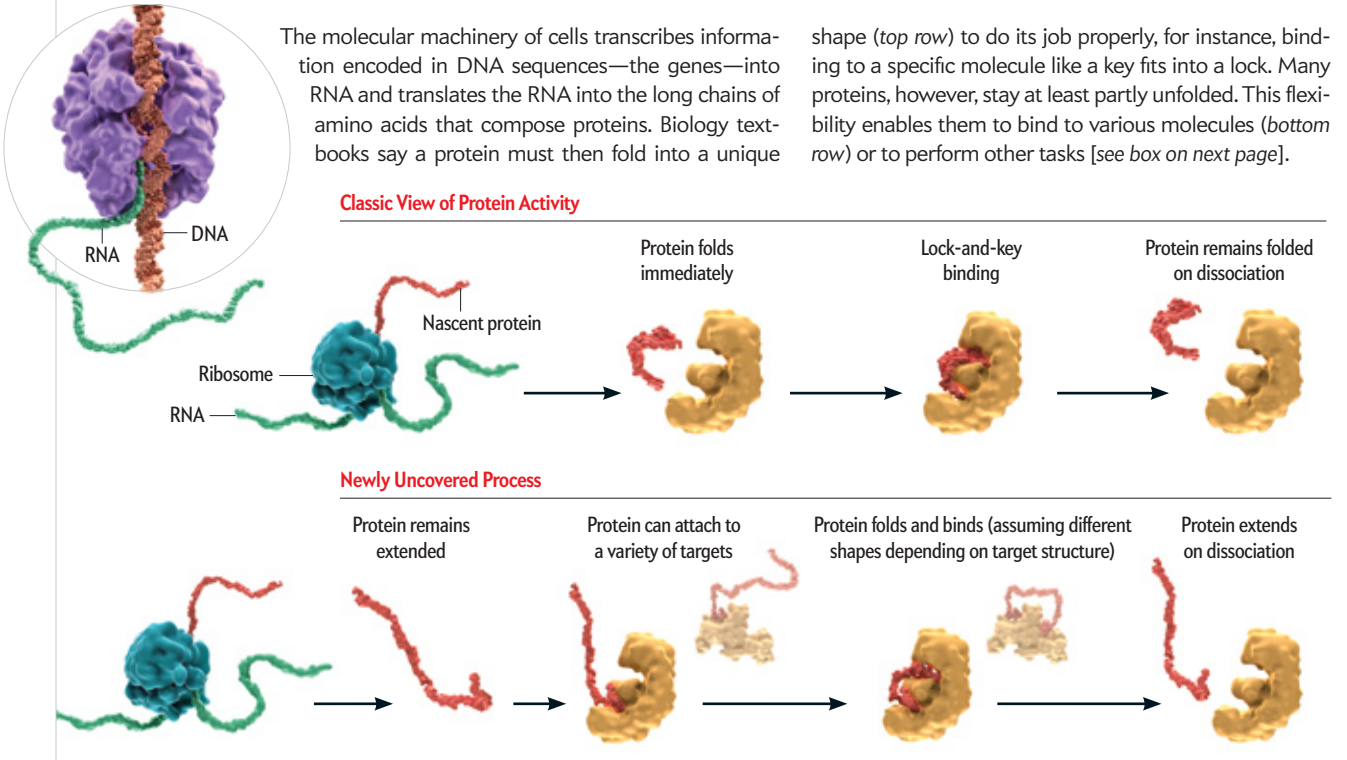
PROTEIN SPAGHETTI

THIS NEW, BROADER VIEW is well illustrated by the protein p27, which is known to exist in most vertebrates. Like p21, p27 is one of the crucial proteins that regulate cell division so that cells do not multiply uncontrollably. NMR shows that p27 is highly flexible, with sections that rapidly fold and unfold into short-lived corkscrew- or sheet-shaped structures. Most cancer cells in humans have reduced amounts of p27, and the greater the loss, the poorer the prognosis for a patient's survival.

The p27 molecule acts as a brake on cell division by binding to and inhibiting the activities of at least six different types of kinase enzymes. Kinases are the master regulators of DNA replication and cell division. They attach phosphate (PO_4) to other proteins ("phosphorylate" them), a move that sets off a cascade of events. In carrying out its task, the stringlike, dynamic p27 molecule wraps around a kinase—which has a mostly rigid structure—and covers a significant portion of its surface, including its chemically reactive, or "active," sites [*see illustration on preceding pages*]. This blockage prevents phosphorylation and so arrests cell division. Thanks to its flexibility, then, p27 can mold itself around, and inhibit, different types of enzymes. Proteins with

Order vs. Disorder

The molecular machinery of cells transcribes information encoded in DNA sequences—the genes—into RNA and translates the RNA into the long chains of amino acids that compose proteins. Biology textbooks say a protein must then fold into a unique shape (*top row*) to do its job properly, for instance, binding to a specific molecule like a key fits into a lock. Many proteins, however, stay at least partly unfolded. This flexibility enables them to bind to various molecules (*bottom row*) or to perform other tasks [*see box on next page*].



such an ability are described as promiscuous or moonlighting.

The p27 protein, being almost completely unstructured, falls near the disordered end of a scale that ranges from complete disorder (totally unstructured) to complete order (totally rigidly folded). The kinases themselves fall near the opposite end of this scale. Many other proteins lie somewhere in between, having both structured and unstructured regions. Calcineurin, which is involved in immune responses (and is the target of antirejection drugs), is the reverse of a kinase: it removes phosphates from particular proteins that have been phosphorylated. It has a structured region that is the enzyme's active site and operates in the classic lock-and-key-manner to remove phosphates from other proteins. But it also has an unstructured region that binds to and inactivates the enzyme's own active site when phosphate removal is not needed. Thus, calcineurin is like two proteins in one: the structured region performs catalysis, and the unstructured region regulates this catalytic function.

The examples we have discussed so far are proteins that fold—either on themselves or around other proteins—when they perform their function. But disorder is often part of a protein's working gear. In one known example, the length of an unstructured region acts as a timing device, controlling how fast two binding sites come together: if the unstructured region is longer, the two binding sites spend more time searching for each other than when the unstructured region is shorter. In another instance, being unstructured enables a particular protein to thread through a narrow opening and cross the cell membrane. And unstructured proteins occur in the axons of nerve cells, where they form brushlike structures that prevent the axons from collapsing.

Unexpectedly, some proteins remain unstructured even after binding. At the Hospital for Sick Children in Toronto, Tanja Mittag (now in the faculty of Kriwacki's department) recently discovered an inhibiting protein in yeast, called Sic1, that stays attached to its partner through several small segments that continuously hop on and off a single binding site, while the rest of Sic1 remains disordered.

Disorder also exists in the proteins of simpler organisms and even of viruses. Some viruses known as phages, which specialize in infecting bacteria, attach to a host's membrane via proteins that connect to the main body of the phage through flexible linkers. The attachment protein, which is smaller and faster-moving than the entire phage, can then rapidly reorient to optimize its alignment during docking.

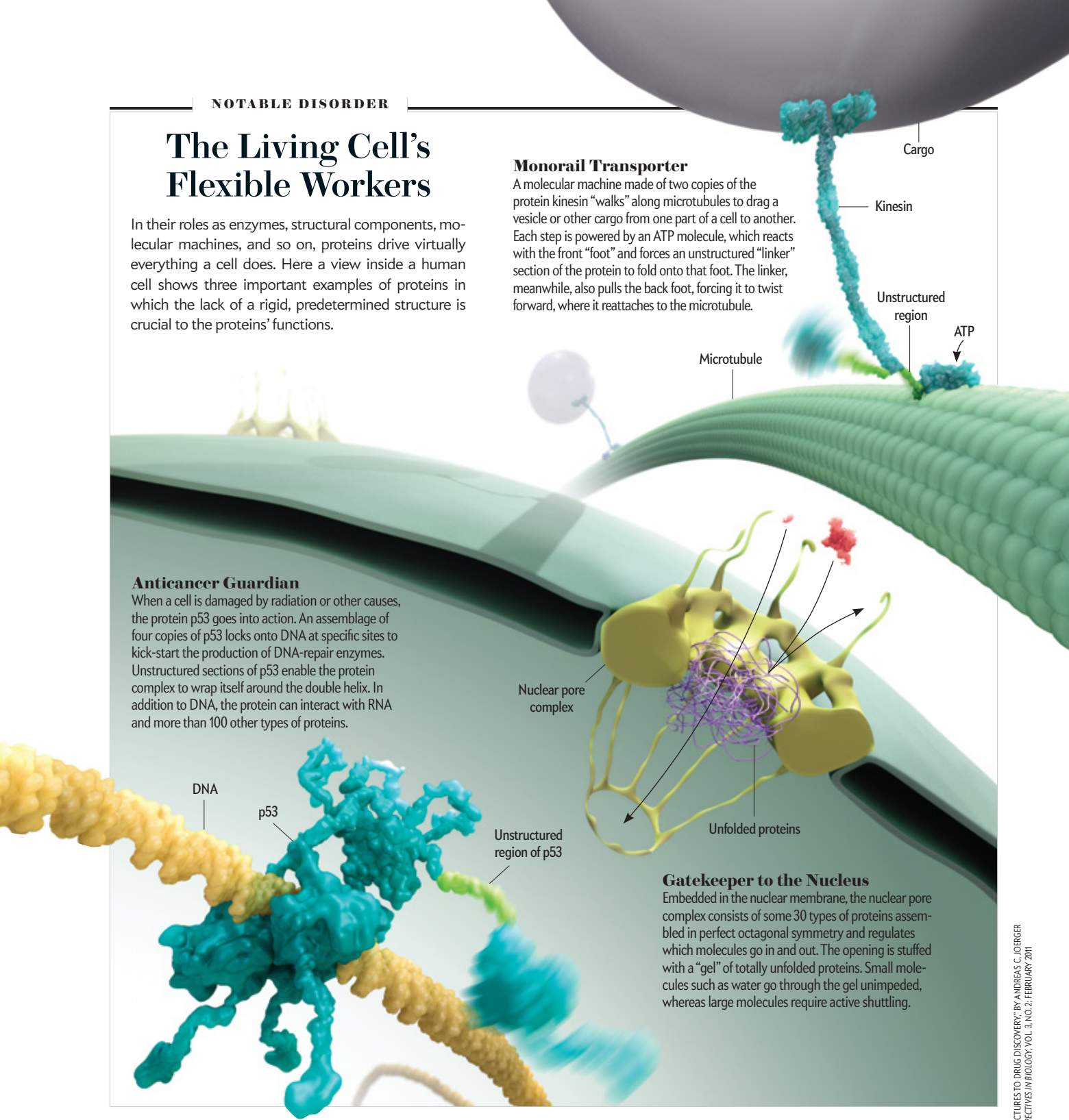
WIDESPREAD PROMISCUITY

TO DATE, ROUGHLY 600 partially or totally unstructured proteins have been directly identified and their functions understood by researchers at laboratories around the world. But we suspect many more exist. After all, scientists have so far learned the structure of just a small fraction of the estimated 100,000 or so proteins that exist in the human body alone. Also, new "bioinformatics" studies by Dunker and his collaborators point in that direction.

The bioinformatics approach builds on earlier theoretical studies of individual proteins, which suggested that after a cell synthesizes a chain of amino acids to make a protein, the chain folds in a way that depends on its composition. In particular, the amino acids that are bulky and hydrophobic—meaning they "dislike" the water molecules that naturally surround proteins—tend to end up in the interior. In contrast, the ones that end up on the surface of a given folded protein are generally small and hydro-

The Living Cell's Flexible Workers

In their roles as enzymes, structural components, molecular machines, and so on, proteins drive virtually everything a cell does. Here a view inside a human cell shows three important examples of proteins in which the lack of a rigid, predetermined structure is crucial to the proteins' functions.



Monorail Transporter

A molecular machine made of two copies of the protein kinesin "walks" along microtubules to drag a vesicle or other cargo from one part of a cell to another. Each step is powered by an ATP molecule, which reacts with the front "foot" and forces an unstructured "linker" section of the protein to fold onto that foot. The linker, meanwhile, also pulls the back foot, forcing it to twist forward, where it reattaches to the microtubule.

Anticancer Guardian

When a cell is damaged by radiation or other causes, the protein p53 goes into action. An assemblage of four copies of p53 locks onto DNA at specific sites to kick-start the production of DNA-repair enzymes. Unstructured sections of p53 enable the protein complex to wrap itself around the double helix. In addition to DNA, the protein can interact with RNA and more than 100 other types of proteins.

Gatekeeper to the Nucleus

Embedded in the nuclear membrane, the nuclear pore complex consists of some 30 types of proteins assembled in perfect octagonal symmetry and regulates which molecules go in and out. The opening is stuffed with a "gel" of totally unfolded proteins. Small molecules such as water go through the gel unimpeded, whereas large molecules require active shuttling.

SOURCE: "THE TUMOR SUPPRESSOR P53: FROM STRUCTURES TO DRUG DISCOVERY" BY ANDREAS C. JOERGER AND ALAN R. FERSHT, IN *COLD SPRING HARBOR PERSPECTIVES IN BIOLOGY*; VOL. 3, NO. 2; FEBRUARY 2011

philic—they tend to stick to the surrounding water molecules.

Dunker's idea was to compare the amino acid sequences of proteins known to be intrinsically disordered with those of proteins known to have rigidly folded shapes. What his team found in 1997, using computer algorithms, was that intrinsically disordered proteins tend to be richer in hydrophilic amino acids when compared with rigid proteins. Thus, the balance of hydrophilic and hydrophobic amino acids could predict whether a given protein would fold only partially or not at all.

To explore the biological implications of its earlier findings, in 2000 Dunker's team made a comparison across the kingdoms of life. The researchers examined the genomes of various organisms with algorithms that looked for stretches of DNA coding for long chains of hydrophilic amino acids. The corresponding proteins would be top candidates to be at least partially unstructured. In the simplest organisms, bacteria and archaea, fewer proteins were predicted to be intrinsically disordered. But in eukaryotes—the more complex organisms such as yeast, fruit flies

and humans, which have nucleated cells—unstructured proteins seem to be much more prevalent.

These results were extended in 2004 by a team led by David T. Jones of University College London, who used similar comparisons that included human data. Strikingly, the investigators found that as many as 35 percent of all human proteins may have long unstructured regions. Thus, about one third of our proteins may have large regions for which the lock-and-key concept is simply irrelevant.

The reasons for this discrepancy are unclear, but a possible explanation is that proteins with lock-and-key structural features are optimized for functions such as enzymatic activity, whereas intrinsically disordered proteins are best at signaling and regulation. Simple bacteria have everything in one container; complex organisms have multiple intracellular containers such as the nucleus, the Golgi, the mitochondria, and so on and thus need more signaling among their various parts and require more extensive regulation. Multicellular organisms also require signaling schemes to coordinate actions among various cells and tissues. In the example of p27 discussed earlier, thanks to its flexibility the protein can carry chemical messages along a cell's signaling pathways: the messages are encoded in its conformation, in its chemical modifications such as phosphorylation, and in the partners it binds to (and thus inhibits or regulates).

EVOLUTION'S BEST-KEPT SECRET

THE DEARTH of intrinsically disordered proteins in bacteria might seem to imply that these proteins arose only late in evolution. Several lines of investigation, however, suggest that they arose early. For one thing, numerous important bacterial signaling systems do use unstructured rather than structured proteins. Furthermore, in evolutionarily ancient molecular machines that are made of RNA and proteins assembled together, nearly all the proteins are partially or entirely unstructured when not bound to their RNA partners. These ancient hybrid complexes include the spliceosome (a molecular machine that edits, or splices, RNA as a step toward producing proteins) and the ribosome (the complex that strings amino acids together into proteins).

VIDEOS OF FLEXIBLE PROTEINS
ScientificAmerican.com/apr2011/flexible-proteins

Research into the origin of life also hints at the antiquity of unstructured proteins. A leading hypothesis is that the first organisms were based on RNA. The RNA acted both as a catalytic molecule and as a repository of genetic information—the roles that in modern cells are played by proteins and DNA, respectively. One significant problem with this "RNA world" theory is that RNA folds very inefficiently into its catalytically active form and often gets stuck in inactive conformations. In today's cells proteins called RNA chaperones help the RNA fold correctly. Other proteins stabilize a given RNA in its active conformation, raising the possibility that the advent of such proteins solved the sticking problem of RNA folding. Both the chaperone and the stabilizer proteins lack stable structure before binding to RNA.

Yet more support for the early evolution of unstructured proteins comes from analyzing the origin of the genetic code. The genetic code is the set of rules cells use to translate the information stored in nucleic acids (RNA or DNA) into an amino acid sequence. Researchers believe that certain amino acids were encoded early in the evolution of life, whereas others came later. The bulky, hydrophobic amino acids that drive a protein to fold likely came late, so proteins made from just the early amino acids would very likely remain unfolded if left alone. If these ideas on the evolution of the genetic code are correct, then the first proteins on earth folded poorly or not at all. The amino acids that arose later evidently enabled proteins to form structure, providing the basis for the formation of lock-and-key enzyme active sites and enabling proteins, over millions of years, to replace RNA as the catalytic powerhouse in all living cells.

DOUBLE-EDGED SWORD

GIVEN HOW CENTRAL proteins are to biology, it should be no surprise that many of them are involved in disease. The new paradigm of intrinsic disorder in proteins will thus profoundly affect how we understand and treat human illnesses.

For starters, in some cases a protein's lack of structure may be harmful: if a cell produces them in excess, certain unstructured proteins are prone to jumble up and form plaques. In the brain, such plaques are major suspects in several devastating neurodegenerative diseases, including Alzheimer's, Parkinson's and Huntington's. More generally, it seems unstructured proteins need to be kept scrupulously in check to avoid trouble: a large-scale study of yeast, mice and humans led by M. Madan Babu of the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England, showed in 2008 that cells regulate disordered proteins more tightly compared with folded proteins.

The realization that intrinsically disordered proteins can be involved in certain diseases is also leading to new ideas for potential treatments. Protein-protein interactions underlie virtually every biological process and thus have long been attractive targets for drug discovery, but with little success so far, compared with the approach that targets interactions of enzymes with smaller molecules. Proteins that interact with unstructured proteins often offer their partners anchoring nooks, which researchers might exploit to insert new drugs. In particular, molecules that block an interaction between an important gene for suppressing cancer and one of its regulatory partners have shown success at fighting cancer in lab animals and are now undergoing clinical trials in humans. Kriwacki, with his colleagues, is developing a similar line of attack to treat retinoblastoma, a cancer of the eye that especially affects children. Early tests in animals have given promising results. Other labs are working on similar projects.

Scientists interested in understanding how proteins work are beginning to dispel past biases represented by the lock-and-key model of protein function. They are recognizing that some biological functions are best performed by rigid proteins and others by highly dynamic ones. The dawning of a new era in protein structure and function has the potential to transform our understanding of life—and perhaps to save a life. SA

MORE TO EXPLORE

Structural Studies of p21$^{Waf1/Cip1/Sdi1}$ in the Free and Cdk2-Bound State: Conformational Disorder Mediates Binding Diversity. Richard W. Kriwacki et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 93, No. 21, pages 11504–11509; October 15, 1996.

Identification and Functions of Usefully Disordered Proteins. A. Keith Dunker et al. in *Advances in Protein Chemistry*, Vol. 62, pages 25–49; 2002.

Intrinsically Unstructured Proteins and Their Functions. H. Jane Dyson and Peter E. Wright in *Nature Reviews Molecular Cell Biology*, Vol. 6, pages 197–208; March 2005.

Structural Disorder Throws New Light on Moonlighting. Peter Tompa et al. in *Trends in Biochemical Sciences*, Vol. 30, No. 9, pages 484–489; September 1, 2005.

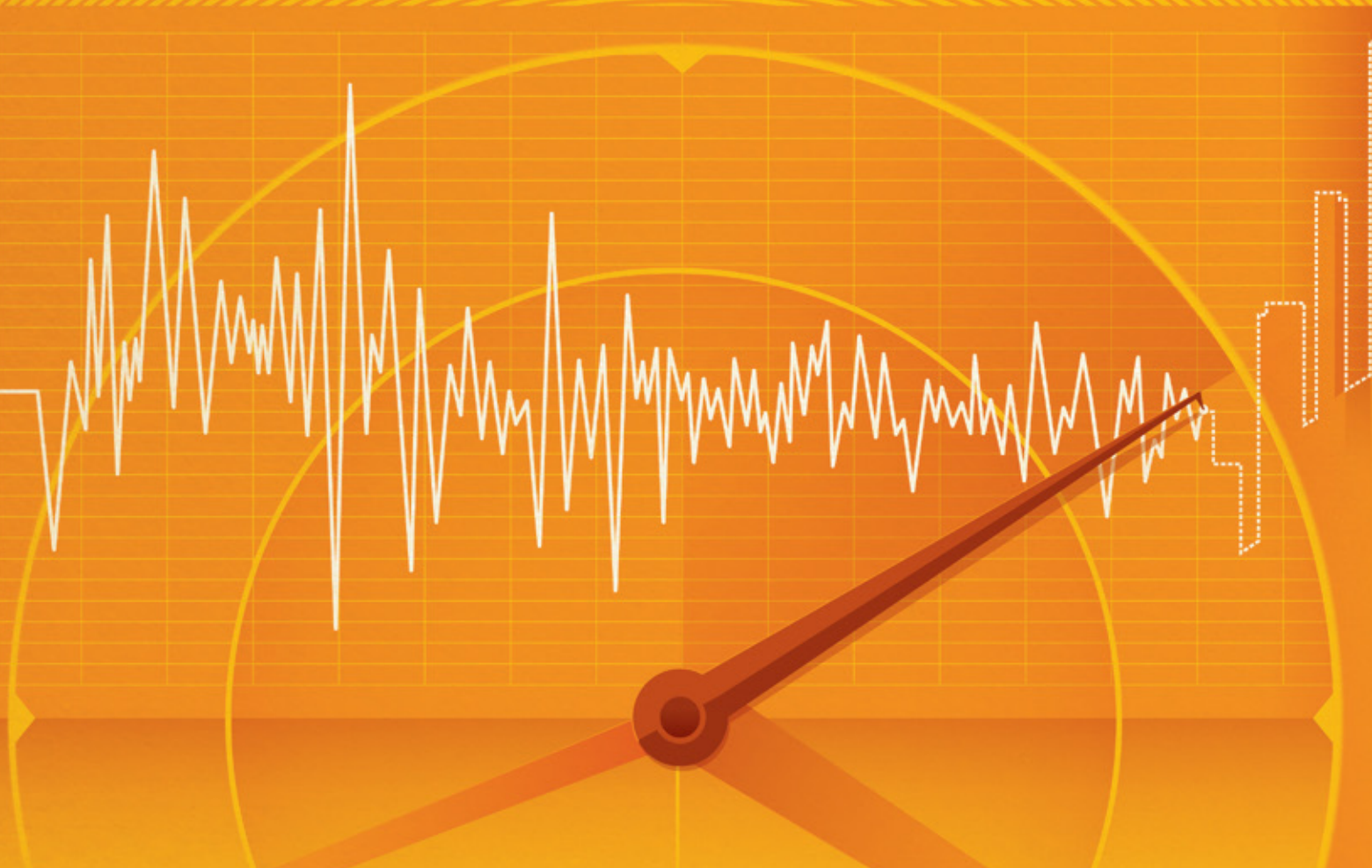
Database of Protein Disorder. Known unstructured proteins are searchable online at www.disprot.org. **Protein Data Bank** (www.rcsb.org/pdb) is a database of structured proteins.

SEISMOLOGY

SECONDS BEFORE THE BIG ONE

Earthquake detection systems can sound the alarm in the moments before a big tremor strikes—time enough to save lives

By Richard Allen



IN BRIEF

Earthquake early-warning networks detect the earliest stages of an earthquake and sound an alarm to warn people of the danger. The alerts can provide tens of seconds of warning time.

Most systems rely on the fact that an earthquake comes in two parts: a fast-moving, sudden jolt and a slower-moving wave that causes the great majority of the damage.

A network of seismometers can quickly identify the earthquake's epicenter, improve predictions of the earthquake's magnitude and reduce the incidence of false alarms.

These networks already exist in a number of countries around the world. A proposed system for California would protect individuals and businesses up and down the Golden State.

Illustration by Tom Whalen

Richard Allen is a professor of geophysics and associate director of the seismological laboratory at the University of California, Berkeley. He is currently testing a prototype earthquake early-warning system that could be extended to all of California.

EARTHQUAKES ARE UNIQUE IN THE PANTHEON OF NATURAL DISASTERS IN THAT THEY PROVIDE NO warning at all before they strike. Consider the case of the Loma Prieta quake, which hit the San Francisco Bay Area on October 17, 1989, just as warm-ups were getting under way for the evening's World Series game between the San Francisco Giants and the Oakland A's. At 5:04 P.M., a sudden slip of the San Andreas Fault shook the region with enough force to collapse a 1.5-mile section of a double-decker freeway and sections of the Bay Bridge connecting Oakland with San Francisco. More than 60 people died.

Over the years scientists have hunted for some signal—a precursory sign, however faint—that would allow forecasters to pinpoint exactly where and when the big ones will hit, something that would put people out of harm's way. After decades spent searching in vain, many seismologists now doubt whether such a signal even exists.

Yet not all hope is lost. Within seconds of an earthquake's first subtle motions, scientists can now predict with some certainty how strong and widespread the shaking will be. By integrating new science with modern communications technologies, the authorities could get a few tens of seconds' warning, perhaps even half a minute, to those in harm's way. That may not sound like much, but it is enough to send shutdown warnings to power plants and rail networks, automatically open elevator doors and alert firefighters.

The Loma Prieta quake was centered south of the Bay in the rugged Santa Cruz Mountains. After the ground started to shake, it took more than 30 seconds for the damaging vibrations to travel the 60 miles to San Francisco and Oakland, the scenes of more than 80 percent of the fatalities. If an earthquake early-warning system had existed back then, it could have provided perhaps a 20-second warning to the heart of the region. This is enough time to slow and stop trains, issue "go around" commands to airplanes on final approach and turn streetlights red—preventing cars from entering hazardous structures such as bridges and tunnels. Workers in hazardous work environments could move to safe zones, and sensitive equipment could enter a hold mode, reducing damage and loss. Schoolchildren and office workers could get under desks before the shaking arrived. The region would be ready to ride out the violence to come.

Such networks are being deployed all over the world in locations as diverse as Mexico, Taiwan, Turkey and Romania. Japan's system is among the most advanced. The nationwide network issues warnings via most television and radio stations, several cell phone providers, and the public address system of malls and other public spaces. In the three and a half years since the system came online, more than a dozen earthquakes have already triggered widespread alerts. People in factories, schools, trains and automobiles were given a few precious moments to prepare; following the alerts, there were no reports of panic or highway accidents. The U.S. is behind the rest of the world, but a new test bed being deployed in California should soon lead to a full-scale warning system in that fault-ridden state.

California is long past due for the next big one. If we build a warning system now, we can save lives.

FROM WAVES TO WARNINGS

THE GROUND BENEATH OUR FEET is moving. As the tectonic plates drift across the earth's surface, pieces of the continents grind past one another and collide like cars in a freeway pileup. The earth's crust—the outer layer of the plates that we live on—is elastic, but only to a point. At the plate boundaries, the crust bends until the strain becomes too great. When it snaps, the energy stored up over the preceding decades tears across the earth's surface, shaking everything in its path.

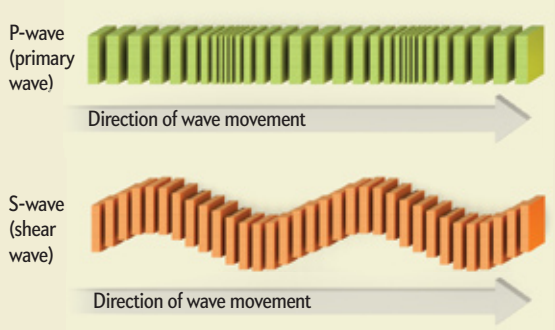
Hundreds of earthquakes occur every day. Fortunately, most are so small that we would never know about them without the help of sensitive seismometers. In daily earthquakes only three to six feet of the fault plane slips; humans cannot feel the shak-

HOW IT WORKS

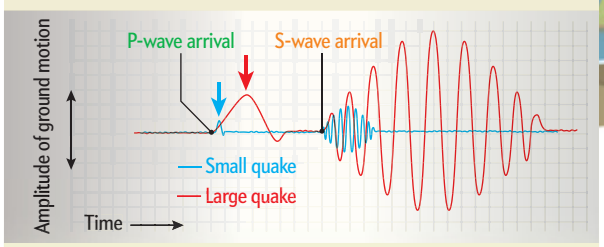
Ready to Rumble

Earthquake early-warning systems detect the first quiverings of a major quake, triggering alarm systems in advance of the most violent shaking. The ShakeAlert system that has been proposed for California would use a network of digital seismometers deployed around the state (*above right*) to give populated areas up to a minute of advance warning (depending on the location of the epicenter). The alerts would allow businesses, residents and public agencies time to get ready (*below right*).

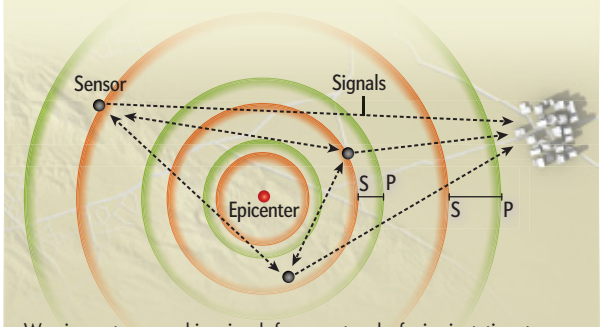
The Science of Earthquake Early Warning



All earthquakes are made of two types of wave. The P-wave compresses the earth as it moves, like a sound wave. It moves fast but does not cause much damage. The S-wave that follows deforms rock up and down like an ocean wave. It delivers most of the tremor's violent energy.



Hundreds of small earthquakes happen every day, so warning systems identify the big ones by checking the shape of the P-wave. Small quakes have a short, sharp pulse (*blue arrow*), whereas big quakes announce themselves with a high-amplitude low-frequency jolt (*red arrow*).

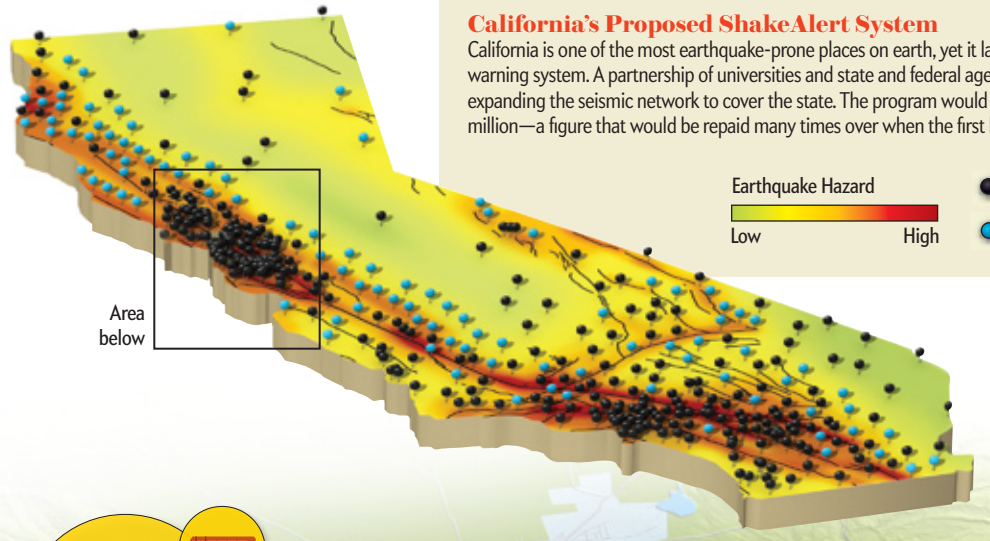


Warning systems combine signals from a network of seismic stations to correlate big jolts and identify the epicenter. The system then sends an electronic alert ahead of the S-wave. As more stations detect shaking, magnitude and epicenter predictions become more refined.

Illustrations by Emily Cooper and Tom Whalen (icons)

California's Proposed ShakeAlert System

California is one of the most earthquake-prone places on earth, yet it lacks even a basic warning system. A partnership of universities and state and federal agencies has proposed expanding the seismic network to cover the state. The program would cost just $80 million—a figure that would be repaid many times over when the first big quake strikes.



Commuter rail systems would automatically brake, reducing the chance of derailment

Manufacturing plants would stop operations and switch equipment into a safe mode

Construction sites would alert workers to move out of the most dangerous locations

Elevators in high-rise buildings would stop at the nearest floor and open their doors

Schools would sound an audible alarm, giving students time to get under their desks

Mobile phones and personal computers would light up with personalized alerts

Airplanes on approach to area airports would be given last-minute "go around" signals

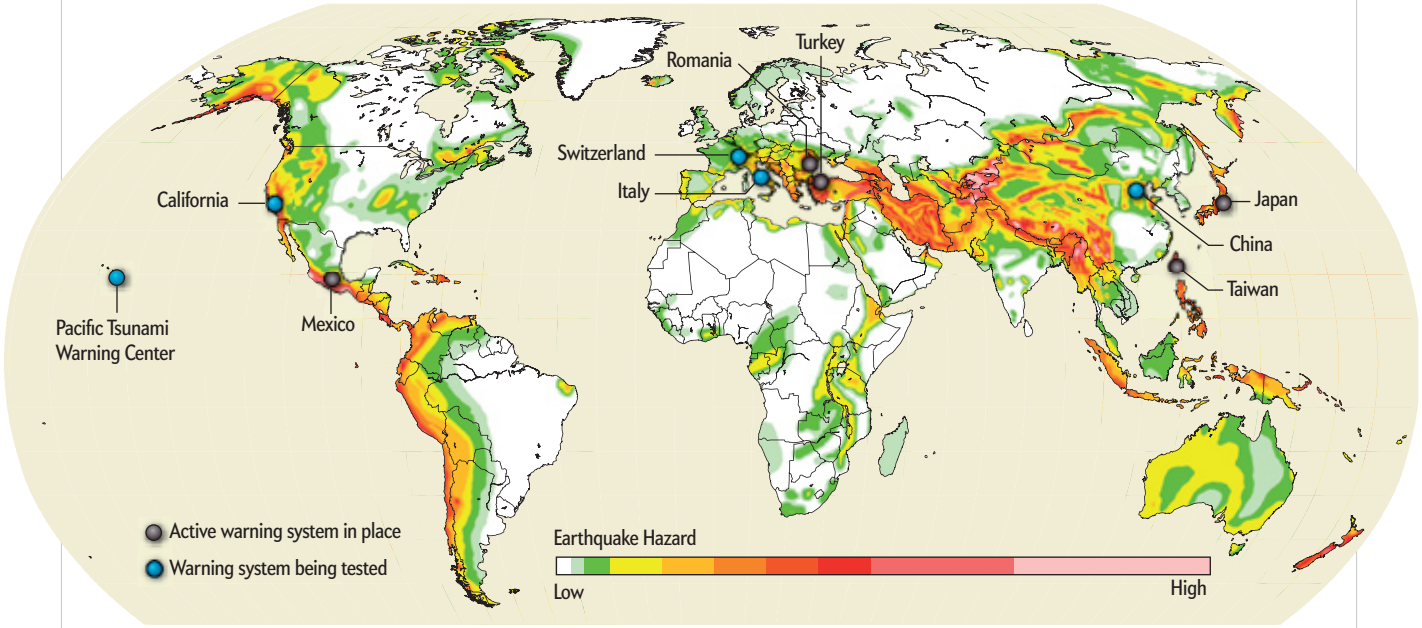
40 seconds
30 seconds
20 seconds
Warning time: 10 seconds
No warning
Epicenter
Oakland
San Francisco
San Mateo
Fremont
San Jose
Santa Cruz
Gilroy
Salinas
Modesto

Sounding the Alarm

Once an earthquake warning system detects a strong quake, the alert goes out. In this scenario, when a break of the San Andreas Fault south of the Bay Area creates a strong tremor, those in the most densely populated areas to the north would have more than half a minute to get ready.

Worldwide Warnings

Currently five earthquake early-warning systems are in place around the world, each tailored to the specific topography of the country in which it is located. In Mexico, sensors on the Pacific coast detect quakes that begin in the subduction zone offshore and trigger alarms in Mexico City, a megalopolis of 20 million people built on tremor-amplifying silt. Similarly, Romania's system is designed to provide the capital of Bucharest with advanced warning of quakes that begin in the southeastern Carpathian Mountains 100 miles away. In contrast, the entirety of Japan is earthquake-prone. After the 1995 earthquake in Kobe that killed more than 6,000 people, the country installed more than 2,000 seismic stations to provide countrywide coverage. It is now the most advanced warning system on the planet.



ing. In magnitude 5.0 earthquakes a mile or two of the fault plane ruptures; humans can easily feel movement, but modern buildings can withstand it. At magnitude 8.0 the rupture propagates for hundreds of miles across the fault plane, and the tear can extend up to the surface. It will rip a building in two.

By monitoring the buildup of strain between earthquakes, seismologists know that many areas of the crust are close to failure. But the detailed structure of the faults deep below the surface also plays an important role in both the nucleation and propagation of earthquake ruptures—a structure that cannot be sampled directly. For this reason, most seismologists do not believe it is possible to create a forecasting system capable of predicting a large earthquake hours or days before it strikes. For the foreseeable future, the best anyone will be able to do is to quickly detect a large earthquake and sound the alarm.

A few unique characteristics of earthquakes aid in this task. What we perceive as one extended jolt actually comes in stages. Energy from a break in the crust travels through the earth in two forms: P-waves and S-waves [*see box on page 76*]. Both types leave the fault surface at the same time, but there the similarities end. P-waves, like sound waves, are compression waves. They travel relatively quickly, but they do not carry much power. During an earthquake, you feel the P-waves as a sudden, vertical thump. S-waves are more like ocean waves, slow movers that contain most of the energy and bring the strongest shaking. The ground motion is horizontal and vertical, and they can bat entire buildings around like they were dinghies in the surf.

In addition, not all waves look alike; they take on different shapes depending on the size of the slip patch. The P-wave radiation for small slip patches has relatively low amplitude and high frequency—a small but sharp pulse. Bigger earthquakes rupture larger areas of a fault and have more slip, so the P-wave is larger in amplitude and lower in frequency. It is akin to the difference between the squeak of a small bird and the roar of a grizzly bear.

A single seismometer could estimate the magnitude of the earthquake based on just this information. Any P-wave with high amplitude and low frequency would trigger a warning. This single-station approach is the fastest way to give warnings near the epicenter. Yet the character of earthquake ruptures varies—not all magnitude 5.0 earthquakes look the same—and the specific sediments underneath the seismometer modify the P-wave. This variability increases the risk of both false alarms—warnings when there is no earthquake—and missed alarms when a damaging earthquake is under way.

To reduce the likelihood of both false and missed alarms, we can combine data recorded by several seismometers located a few miles apart. In this setup the sediments beneath each instrument would be different, so we can obtain an average estimate of the magnitude. This approach requires seismic networks

FROM "THE STATUS OF EARTHQUAKE EARLY WARNING AROUND THE WORLD: AN INTRODUCTORY OVERVIEW," BY RICHARD M. ALLEN, PAOLO GASPARINI, OSAMU KAMIGAICHI AND MAREN BOSE, IN *SEISMOLOGICAL RESEARCH LETTERS*, VOL. 80, NO. 5, SEPTEMBER/OCTOBER 2009

that transmit instrument data to a central site and then integrate them. Yet it takes a few seconds to transmit and analyze the data, and in every passing second the damaging S-wave travels another two to three miles.

The best approach is thus to combine the single-station and network-based approaches, which provides the potential for both rapid warnings in the region near the epicenter and tens of seconds of warning to locations farther away.

As a result of the warning, officials were able to stop the metro 50 seconds before the shaking arrived, and schools were evacuated as planned.

Any system has to make a trade-off between the accuracy and the warning time available. As the seismic network collects more data on an earthquake, the predictions will improve, but the time until shaking will decrease. Some users may tolerate more false and missed alarms to have more warning time. For example, schools may prefer to get the warning sooner so children can take cover. A few false alarms a year provide the regular drills necessary so that everyone knows what to do. Nuclear power stations, in contrast, require only a second to shut down the reactor—but doing so comes at great cost. Operators there will want to wait until extreme shaking is certain.

ALERTS NEAR AND FAR

PUBLIC EARTHQUAKE WARNING SYSTEMS have existed in one form or another for decades. In the 1960s Japanese engineers built seismometers into the tracks of the new Shinkansen bullet trains. Excessive shaking would sound an alarm, giving the conductor a chance to slow the train. Later, scientists designed systems that would use far-flung seismometers to relay warnings in advance of the heaviest shaking. Mexico's network is designed to detect earthquakes near the coastline and broadcast warnings in Mexico City, an aging metropolis of more than 20 million people built on a silty lakebed that amplifies seismic waves. The distance between the coast and the city can provide more than 60 seconds of warning.

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Mexico's system came online back in 1993. Two years later it would experience its first serious test. On October 9, 1995, a magnitude 8.0 earthquake struck just off the coast of Manzanillo. The warning system picked up the tremor and broadcast alerts on television and radio stations in Mexico City and via a dedicated radio alert system similar to weather radio in the U.S. As a result of the warning, officials were able to stop the metro system 50 seconds before the shaking arrived, and schools were evacuated as planned.

Japan's system, which went live in 2007, makes heavy use of personal technology. Alerts go out not only on television and radio but through special receivers in homes, offices and schools. Pop-up windows on computers show a real-time map with the epicenter's location and the radiating seismic waves. A timer counts down to the shaking at your location and highlights predicted intensity. Cell phone providers broadcast a text message–like warning to all phones with a characteristic audible alarm. Critical industries such as nuclear power stations, rail systems, airports and hazardous manufacturing facilities use dedicated communications systems tailored to their needs.

Japan's experience shows that earthquake warning systems do not just help protect lives, they also help the bottom line. In 2003 two earthquakes near Sendai, Japan, caused more than $15 million in losses to the OKI semiconductor manufacturing plant because of fire, equipment damage and loss of productivity. The plant had to be shut down for periods of 17 and 13 days, respectively, following the quakes. The company then spent $600,000 to retrofit the factory and to install a warning system. In two similar earthquakes since, the factory suffered only $200,000 in losses and 4.5 and 3.5 days of downtime.

THE CALIFORNIA CURSE

CALIFORNIA IS EARTHQUAKE COUNTRY. In 2006 a consortium of universities and state and federal agencies joined forces to develop ShakeAlert, a warning system for the state. Right now a prototype system links together approximately 400 seismic stations and will soon send alerts to a small group of test users. The finished system will provide not only immediate single-station alerts to those near the epicenter but also widespread network-based alerts to those farther away. If all goes well, alerts will be available within five seconds after the first P-wave hits.

Yet California still has a long way to go before it can be blanketed with a comprehensive network such as Japan's. The 400 existing seismic stations are concentrated around the San Francisco Bay and Los Angeles metropolitan areas, leaving gaps elsewhere [*see box on page 77*]. Even though most Californians live near these two areas, the gaps both slow the system and reduce its accuracy, because it takes longer to detect the P-waves at multiple locations. In Japan instruments are spaced every 15 miles across the entire country. That level of spacing in California would deliver the best system performance, with fewer false and missed alarms and more warning time.

Those alerts, like Japan's, would leverage the networked gadgets that most people carry every day. Individuals would get an alert on their mobile phone indicating predicted shaking intensity, a countdown until the shaking starts, and perhaps a simple instruction such as "get under a table" or "move to your safe zone." Larger organizations with infrastructure spread over a region will likely want more detailed information such as a real-time map showing the wave progression and the distribution of ground shaking across the affected area.

Such a system would require only a modest investment compared with the potential dangers of a major earthquake—100 new seismic stations and upgrades to existing infrastructure, at a total cost of $80 million. In five years the system could be up and running. In six we could be very thankful that it is. SA

MORE TO EXPLORE

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California Integrated Seismic Network: **www.cisn.org**

SUSTAINABILITY

Food Fight

Genetically modified crops, says agro-research czar Roger Beachy, receive an unjustified shellacking from environmentalists

Interview by Brendan Borrell

ROGER BEACHY GREW UP IN A TRADITIONAL AMISH family on a small farm in Ohio that produced food "in the old ways," he says, with few insecticides, herbicides or other agrochemicals. He went on to become a renowned expert in plant viruses and sowed the world's first genetically modified food crop—a tomato plant with a gene that conferred resistance to the devastating tomato mosaic virus. Beachy sees no irony between his rustic, low-tech boyhood and a career spent developing new types of agricultural technologies. For him, genetic manipulation of food plants is a way of helping preserve the traditions of small farms by reducing the amount of chemicals farmers have to apply to their crops.

In 2009 Beachy took the helm of the National Institute of Food and Agriculture, a new research arm of the U.S. Department of Agriculture, where he controls a $1.5-billion budget for pursuing his vision of the future of agriculture. In the past year Beachy's institute has funded ambitious agricultural research, such as a massive genomic study of 5,000 lines of wheat and barley, alongside unexpected projects: a $15-million behavioral study on childhood obesity in rural states, for one.

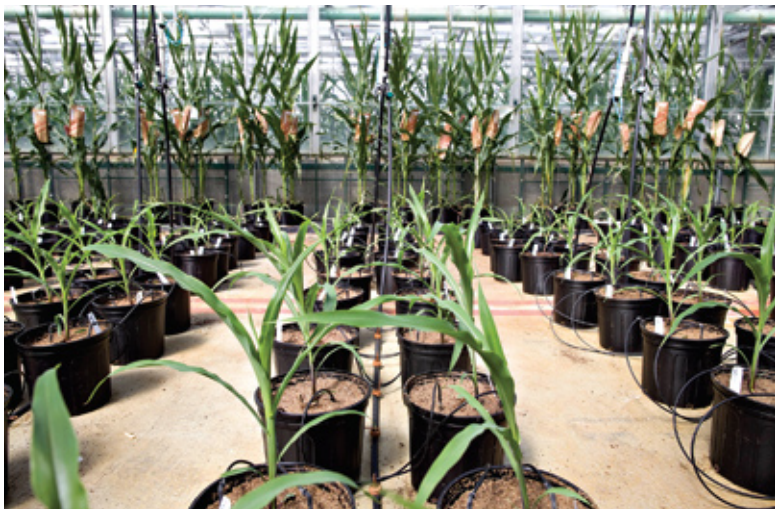
Beachy's appointment sparked controversy among environmentalists because his work helped to kick-start the $11-billion global agricultural biotechnology industry. Seed companies never commercialized his virus-resistant plants, but their success—tomato plants that showed near-complete resistance to multiple virus strains—underlined the potential for a technology that was ultimately widely embraced by U.S. farmers. Today in the U.S. more than 90 percent of soybean and cotton crops and more than 80 percent of corn plants are genetically engineered to resist herbicides and insects using methods similar to the ones developed

IN BRIEF

A pioneer in developing genetically modified foods has assumed an influential role as head of the U.S. Department of Agriculture's research agency.
Roger Beachy continues to advocate for a prominent place for genetic engineering of crops, which he claims provides a basis for chemical-free, sustainable agriculture that will prove more of a boon for the environment than have conventional weed and pest control.
Detractors of GM foods, meanwhile, have expressed their chagrin at Beachy's appointment.
Without GM crops, Beachy contends that farmers would need to return to older practices that would produce lower crop yields, higher prices and an increase in the use of agrochemicals inimical to health.

Photograph by Spencer Heyfron

by Beachy. Organic farmers and locavores worry about Beachy's ties to big agriculture—much of his tomato work received funding from Monsanto—and his advocacy of genetic modification of food crops. Beachy, though, remains unrepentant. Although he believes seed companies can do more to improve food security in the developing world, he insists that genetic manipulation is essential to feed the earth's growing population sustainably. Edited excerpts of a phone conversation with Beachy follow.



GM corn accounts for more than 80 percent of the U.S. plantings of this crop.

SCIENTIFIC AMERICAN: Did you actually get to see the first GM tomatoes when they were planted in the field in Illinois in 1987?

BEACHY: Oh, my goodness, I planted them. I went out and hoed them. I was out there once a week looking at everything in the field, and my daughter K. C. even helped me weed the tomato patch one time. I really wanted to observe the patch and see how it was progressing.

Were you surprised by how effective the virus-resistance gene was?

Absolutely. As the parental plants without the resistance gene were getting sicker and sicker, the ones that had the gene looked just dynamite. I still have the original photos from 25 years ago, and it's pretty remarkable even now to look at them and say, "By George, our stuff really works!" Other people have seen the same kind of technology work in cucumbers and papaya and squash and green peppers; many are surprised at how relatively simple the concept was and yet how much of an impact it can have.

That effectiveness does not last forever, of course. Today we are seeing the resistance these technologies provide against pests and disease being overcome. Do you think the industry has relied too much on GM as a "silver bullet"?

No, these things happen in plant breeding of all kinds, whether it's traditional breeding or molecular breeding like we're doing now. In the 1960s and 1970s new types of wheat rust spread up from Mexico on the wind, and the plant breeders would hustle and hustle to find resistance to one strain of rust, and then, several years later, another strain would come, so they would have to be looking ahead to find any new resistance.

Durable, permanent resistance is almost unheard of, which brings up the question of why did we create GM crops in the first place? What we've gotten over the past 15 to 20 years is a considerable amount of insecticides not being used in the environment. That's remarkable. What we're wondering now is if we will go back to using only chemicals or if we will be able to find new genes that will capture the diversity of pests that we're seeing around the world.

Unlike in the U.S., tropical regions of the world, including parts of China, face constant pressure from multiple insects. To control the variety of crop-damaging insects, scientists will need a variety of different genetic technologies, or it may be necessary to apply nongenetic technologies, such as different proven insecticides to control them. Overall, we'll find the kinds of genes that will protect against white flies in one country and aphids in another country. If we manage this right, we'll have the genetic solutions to these questions and not chemical solutions and will therefore, in my opinion, be more sustainable.

Critics of the agricultural biotechnology industry complain that it has focused on providing benefits to farmers rather than improving foods for consumers. What do you say to them?

In the early years many of us in the university community were looking at using genetic engineering to enhance vitamin content of foods, improve the quality of seed proteins and develop crops that don't require use of pesticides—all things we thought would benefit agriculture and consumers. The process for approval of a biotechnology product was onerous, expensive and unknown for academics. It would take the private sector to make the new technologies successful and find an opportunity to give farmers crops with higher productivity. But the food companies that purchased these crops—General Mills, Kellogg's—were not used to paying more for wheat or oats that had more nutritional content or for vegetables that were higher in minerals.

Why not?

Because the American public would not be willing to pay more for those products.

Today consumers are willing to pay more for crops that are labeled "organic" or even "GM-free" because they view them as more sustainable. How do you think GM crops can help make agriculture more sustainable?

In my opinion, the GM crops we have today already contributed to sustainable agriculture. They have reduced the use of harmful pesticides and herbicides and the loss of soils because they promote the use of no-till methods of farming. Nevertheless, there is much more that can be done. As you know, agriculture and forestry account for approximately 31 percent of global greenhouse gas emissions, larger than the 26 percent from the energy sector. Agriculture is a major source of emissions of methane and nitrous oxides and is responsible for some of the pollution

GETTY IMAGES

of waterways because of fertilizer run-off from fields. Agriculture needs to do better.

We haven't reached the plateau of global population and may not until 2050 or 2060. In the interim, we must increase food production while reducing greenhouse gas emissions and soil erosion and decrease pollution of waterways. That's a formidable challenge. With new technologies in seeds and in crop production, it will be possible to reduce the use of chemical fertilizers and the amount of irrigation while maintaining high yields. Better seeds will help, as will improvements in agricultural practices.

Environmentalists have been reluctant to embrace GM crops because of concerns about genes flowing to non-GM crops and also to wild native plants. That's one reason a federal judge in California recently ordered genetically modified sugar beets to be destroyed.

You are correct. Nevertheless, it is important to note that the court ruling is not about the safety of the sugar beets or the plants that result from cross-pollination. The farmers who brought suit charge a premium for their crops because they are branded as organic—a definition that does not include genetic engineering. They are worried that their non-GM crops will be pollinated by pollen from GM crops, reducing their value. In this case, it is not an issue of food safety but of product marketing.

On the other hand, it's true that there are reasons why we want to preserve wild populations of crop plants: they act as a reservoir for genetic diversity. Here in the U.S., we are not, for instance, planting GM corn alongside wild maize, which is from Mexico. There are some native species for which there is a cross-pollination possibility, for example, squashes and melons, where there are some wild progenitors out in the field. It will be important to ensure that such germplasm is preserved.

In some quarters it might actually be seen as positive if a trait for disease or pest resistance, whether or not it was of GM origin, was transferred to weedy relatives, because it will reduce pests or pathogens in the area.

It may be a positive thing for agriculture, but not necessarily for wild ecosystems. What are the consequences if you create a vitamin A–rich rice and that gene spreads into an environment where vitamin A is scarce?

Most scientists do not predict any negative consequences if the genes used to develop Golden Rice [vitamin A–rich rice] are transferred to other varieties or to wild relatives. In contrast, the payoff for making Golden Rice widely available to those with vitamin A–poor diets is enormous. Imagine if we further delayed the release of such improved foods, leaving many hundreds of thousands of children with blindness and impaired vision and early deaths because of deficiency of vitamin A. What is the value of sight in children? What is the potential damage should the genetic trait be transferred to wild or feral rice? You're right—you can't say that every place in the country or every place in the world or every environment, hot or cold, that it won't have an impact, but we need to weigh the risks and benefits.

FURTHER CONVERSATION
ScientificAmerican.com/apr2011/beachy

Some scientists have complained that biotech companies have stymied research on GM crops. Aren't these studies needed to get accurate answers about the risks of these crops?

That's a complex question with many different factors at play. In my opinion, the field would be more advanced if more academic scientists were involved in testing and other types of experimentation. We've had too little involvement of the academic sector in some of these cases. Many of us urged early on that there be more sharing, and I can understand the concerns of the academics.

On the other hand, I've asked companies why seed isn't made readily available for academic scientists' use. Some point out that there have been a number of academic studies in the past 20 years about using GM crops that were incomplete or poorly designed. And as a result, there was a lot of wasted effort by many other scientists that follow up on such studies.

Take the case of the report that pollen from insect-resistant corn harms larvae of Monarch and other butterflies, which led many to conclude that GM corn would have a devastating effect on Monarch populations. This finding was widely quoted in the media, and the USDA spent a great deal of energy and investment on follow-up research, which in the end showed that Monarch larvae were likely to be affected under very restricted conditions: for example, if the pollination of a crop occurs at the same time and place as the larval growth of the butterfly—a very, very rare occasion.

Furthermore, because the use of insect-resistant corn reduced the use of chemical pesticides, the outcome increased the population of butterflies and other insects. From this and other examples, companies were justifiably concerned about the quality of some academic studies and felt that they had more to lose than to gain in such cases. Yet there is much to be gained from academic scientists conducting well-designed studies with GM crops, and I hope that the future brings greater collaboration and less suspicion between public-sector and private-sector scientists in agriculture biotechnology.

What would be the consequence if GM crops were suddenly removed from the market?

Here in the U.S., there would likely be a modest increase in food prices because the efficiency of food production is currently high as a consequence of using GM traits, resulting in low food prices. We would have to go back to older types of production that would result in lower density of planting and likely lower per-acre outputs. We would likely see an increase in acreage planted, including the use of some marginal lands to increase total output. In the U.S. and other countries, there would be a significant increase in the use of agrochemicals, and the related health issues associated with such use would increase. Although there have been great advances in plant breeding during the past 20 years, the yields of the major commodity crops, such as maize, soybeans and cotton, would be less in the absence of biotechnology than with it. If total global crop production drops, the impacts would, of course, be greater on poorer nations than on those that are wealthier. The agriculturally poor countries would certainly suffer more than those that have a strong foundation of food agriculture production. SA

Brendan Borrell is based in New York City and frequently writes about science and the environment for *Scientific American* and *Nature*.

MORE TO EXPLORE

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Kenneth C. Catania is an associate professor of biological sciences at Vanderbilt University. The recipient of a MacArthur "genius" grant in 2006, he focuses his research on comparative neurobiology, with an emphasis on animal sensory systems. This is his third article for *Scientific American*.

IN BRIEF

The tentacled snake is a small, aquatic snake found in Southeast Asia, so named for the distinctive appendages that project from the sides of its snout.
The purpose of the tentacles has long been a mystery. The author set out to test their function.
Along the way, he discovered that the snake has an arsenal of surprisingly advanced hunting strategies that it deploys from birth—an extreme example of nature, instead of nurture, shaping behavior.

ANIMAL BEHAVIOR

Natural-Born Killer

Lethal from day one, the tentacled snake uses surprisingly sly tactics to capture fish

By Kenneth C. Catania

WE HUMANS ARE PRETTY SMUG ABOUT OUR LARGE brains and sophisticated ways. But if there is one thing I have learned as a biologist, it is to never underestimate the abilities of animals that most people consider primitive and simple-minded. Usually mammals teach me this lesson. But recently the complexity of the behaviors I observed in a peculiar reptile known as the tentacled snake made my jaw drop in amazement.

The tentacled snake, *Erpeton tentaculatus,* is a fully aquatic serpent native to Thailand, Cambodia and South Vietnam. A relatively small snake (adults are about two feet long), it gives birth to live young and feeds exclusively on fish. The animal's name refers to its most distinctive trait: the pair of tentacles that project from the sides of the snout. I first became interested in these creatures around a decade ago on a nostalgic visit to the National Zoo in Washington, D.C., where I had worked summers as an undergraduate. Walking through the reptile house, I came across an aquarium thick with vegetation where a tentacled snake was lying in wait. It hung motionless in the water trying hard to look like a stick, its body curved into the characteristic J shape that the snakes adopt when hunting.

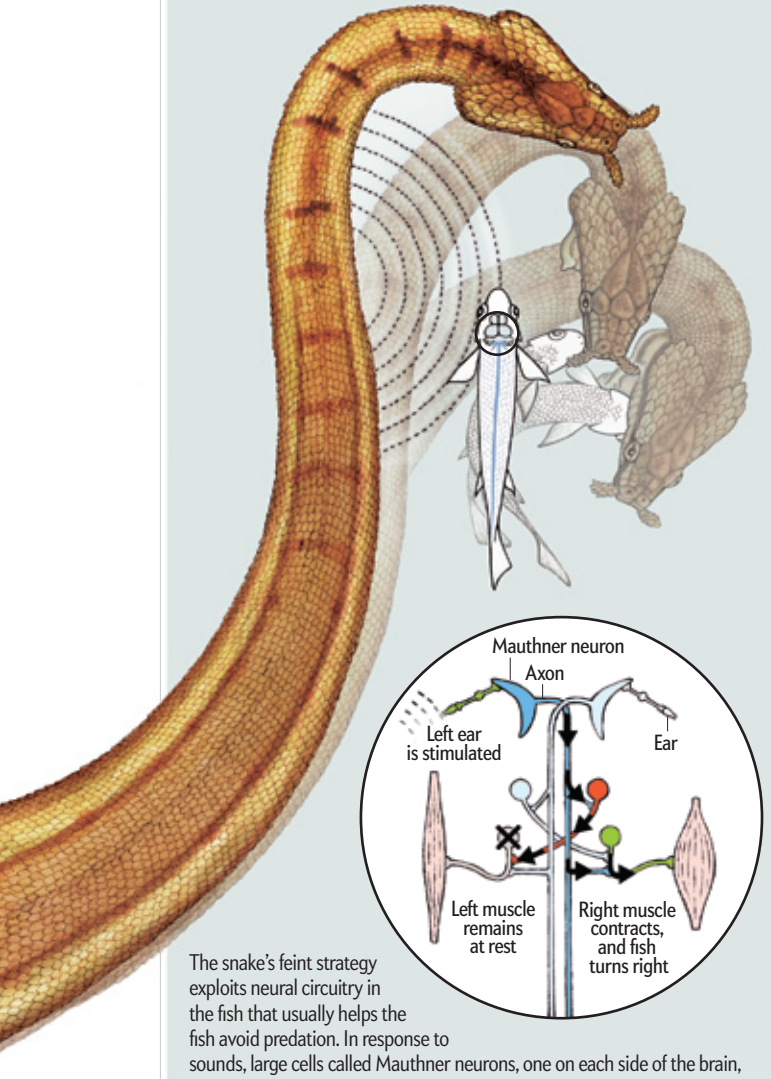
As I watched the snake, I wondered what the tentacles were for. No other snake has anything quite like them. Because these animals feed on fish, it stood to reason that the tentacles might be fish detectors of some kind. But when I returned to my lab at Vanderbilt University and searched the scientific literature, I found that although tentacle theories, including this one, had been proposed, no one had tested them experimentally. So I set out to solve the mystery of the snake's bizarre appendages once and for all.

In my quest to discern the true purpose of the tentacles, I discovered that this animal was even more interesting than I had realized. It turns out that the tentacled snake uses an array of remarkably advanced attack strategies to capture prey. Furthermore, even newborns of this species possess these skills, revealing a dramatic example of nature, rather than nurture, molding behavior.

KENNETH C. CATANIA

Startle and Strike

Tentacled snakes on the hunt curve their bodies into a J shape that creates a trap for unsuspecting fish. When a fish enters the concave area formed by the head and upper body, the snake moves the part of its body directly across from its head, generating a propagation pressure wave. This wave startles the fish into darting in the opposite direction. If the fish is aligned parallel to the snake's jaws during this feint, it may inadvertently swim right into the snake's open mouth. If, however, the fish is already facing the snake's mouth when the feint occurs (*shown*), the snake will predict the fish's escape route and, before the fish even moves, strike at the future location of the fleeing fish's head so that its jaws reach the spot just as the fish arrives.



The snake's feint strategy exploits neural circuitry in the fish that usually helps the fish avoid predation. In response to sounds, large cells called Mauthner neurons, one on each side of the brain, carry signals along their axons to opposite sides of the body, where they cause muscle contractions that turn the fish left or right. A predator-generated sound originating on the left side, for example, will stimulate the left Mauthner neuron, whose axon crosses over to the right side of the body and causes a muscle contraction that steers the animal to the right. Meanwhile inhibitory neurons block muscles on the left from contracting, thus ensuring that the right turn occurs.

IN THE BLINK OF AN EYE

BEFORE I COULD TEST THE THEORY that the tentacles function as fish detectors, I first had to carefully observe the snake's hunting behavior. But watching snakes hunt is not as simple as it might sound. Tentacled snakes strike with incredible speed, and fish are equally fast. The entire contest between snake and fish plays out in about 40 milliseconds, or 1/25th of a second. To see these events, I recorded strike after strike for a number of snakes using a high-speed camera shooting at 500 to 2,000 frames per second and then played the video back in slow motion. As I watched the attacks, I noticed something very strange: seemingly suicidal fish.

In many instances, fish turned toward the approaching jaws of the striking snake, sometimes swimming straight into the snake's mouth. This made no sense. Fish are a top menu item for many predators, and as a consequence, they are expert escape artists, having evolved rapid neural circuits and correspondingly swift behaviors to sense and evade enemies. When they detect the sounds and water motion generated by a predator, they can begin their flight to safety in just six to seven milliseconds—less than 1/150th of a second. This escape response, called a C-start because it starts with a C-shaped bend of the fish's body, is supposed to propel the fish away from a predator on the hunt. Why, then, were fish moving toward the tentacled snake's mouth?

The answer, I found, has to do with the unusual J-shaped hunting posture of the snakes, which forms a trap of sorts. These reptiles prefer to go after fish that have entered the concave area of the J-shaped region formed by their head and upper body. Careful examination of the slow-motion video revealed that just before attacking, the snake moved a portion of its body on the side of the fish farthest from the snake's head, startling the fish toward the predator's open mouth. When I filmed the strikes at 2,000 frames per second and simultaneously recorded sounds in the aquarium with an underwater microphone, I determined that the movement of the snake's body just before the strike creates a propagating pressure wave strong enough to startle a fish.

The snake's feint strategy is particularly insidious, because it taps into the neural circuitry that usually works in favor of fish. Fish have a pair of giant cells in their brain, one on each side, called Mauthner neurons. The neurons' signal-carrying extensions, called axons, cross over to the opposite side of the body. A race between these two fast-conducting neurons determines the direction of the escape response. When a sound originates on the left side, for example, the ears excite the left Mauthner neuron first, which in turn carries a signal down its axon and stimulates motor neurons on the right side of the body, causing a massive muscle contraction that turns the fish to the right. At the same time, inhibitory neurons that cross back over to the left side prevent the muscles on the left from contracting, thus ensuring that nothing interferes with the all-important right turn. The result is an incredibly fast escape—unless the fish swims too close to a tentacled snake. In that case, the snake's body feint usually sets in motion the cascade of neural events that leads to a turn in the wrong direction. And unfortunately for the fish, the simultaneous activation of the inhibitory circuitry that usually functions as a safety means there is no turning back.

The snake's astonishing trick explains some previously puzzling observations. In 1999 John C. Murphy of the Field Museum of Natural History in Chicago reported that fish were eaten very quickly and sometimes disappeared completely during the snake's strike, within one frame of his 30-frames-per-second video—

Illustration by Patricia J. Wynne

much faster than expected. My high-speed videos reveal that even when the fish do not oblige the snake by swimming straight into its mouth, the turn they make toward the snake usually allows it to capture them headfirst, which is the quickest way for a snake to swallow fish. This fast eating not only allows the snake to eat more often, but it also helps to keep the predator's identity under wraps (it is hard to look like a harmless stick if other fish have seen you devour their comrade). Furthermore, the snakes have their own predators and are most likely to be seen themselves when swallowing a fish, so rapid dining may reduce the hunter's chances of becoming the hunted.

MAKING PREDICTIONS

PSYCHOLOGIST B. F. SKINNER once said, "When you run into something interesting, drop everything else and study it." In that spirit, I decided to put my interest in the tentacles aside temporarily and focus on the snake's predatory behavior—a shift that turned up more tricks in the creature's repertoire.

Although startling fish toward a strike is impressive, it works only when the fish is situated in the "sweet spot" between the snake's head and neck and parallel to its jaws. What about fish in other orientations? Because the fish's escape response propels it either to the left or the right, the snake cannot startle a fish toward its mouth if the fish is already facing its jaws. In this case, the tentacled snake employs another, even more impressive strategy: it predicts fish behavior. First it uses a body feint to startle the fish away from its body, sending the fish on a path parallel to the snake's jaws. Then, before the fish even moves, the snake strikes toward the future location of the fish's head, such that its jaws reach the spot just as the ill-fated fish arrives. The events occur far too quickly for the snake to use visual feedback to track the moving fish during the strike—it must plan ahead. In some experimental trials, the fish did not turn away from the body feint (the tactic is not foolproof), yet the snake still struck in the direction the fish should have moved in had it reacted in the usual way. This behavior confirmed that the snake strikes based on prediction, rather than tracking the fish as it moves.

Sometimes snakes simply struck at a fish even if they were unable to startle it in a particular direction. But for the most part, snakes patiently waited for fish to enter the trap formed by their J-shaped hunting posture. To my surprise, I observed yet more kinds of predictive strikes for fish in this zone, depending on the position of the fish. In one contortionistic variant, snakes curled their head under their own body to meet an escaping fish head-on. It seems tentacled snakes can choose from a range of attack strategies in their arsenal, depending on the situation at hand. These predictive strikes raised an interesting question: Do tentacled snakes learn to predict the movements of a C-starting fish from a lifetime of striking, or are they born with this ability? As luck would have it, several of our snakes gave birth. When we tested the newborns with live fish, they clearly struck for the future location of escaping fish (when fish were in the appropriate position), thus showing they were born knowing how a fish moves and how best to outsmart it.

TENTACLED SNAKE VIDEO
ScientificAmerican.com/apr2011/catania

Reporting our findings last year in *PLoS ONE,* we observed that this innate ability testifies to the long evolutionary history of tentacled snakes preying on fish and bears on one of the most fundamental questions in biology—namely, the relative roles of nature and nurture in the development of behavior. Tentacled snakes sit at the extreme nature end of this continuum, at least when it comes to strikes by newborns. The very reliable response of fish to a sudden water disturbance provided a framework for the evolution of one innate behavior (predictive strikes) that takes advantage of another innate behavior (fish-escape responses).

KENNETH C. CATANIA

Scaled tentacles seen in this scanning electron micrograph can sense the slightest water movement, making for an excellent fish detector.

That the fish have not evolved a counterstrategy suggests that tentacled snakes are acting as what Stephen Jay Gould termed "rare enemies," exploiting a behavior that is normally adaptive. Fish have many predators, and most of the time their best bet on detecting a sudden water disturbance is to flee in the opposite direction. It is the unlucky fish that encounters this snake and is tricked into turning toward its enemy rather than away from it.

SEEING IN DARKNESS

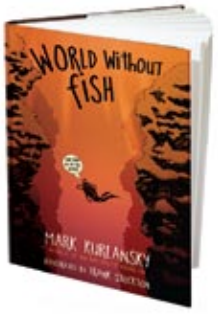
AS FOR THE TENTACLES, my graduate student Duncan B. Leitch and my research assistant Danielle Gauthier and I conducted a series of investigations to determine their function. We published our results in 2010 in the *Journal of Experimental Biology.* By examining the anatomy of the nerve endings in these appendages, their responses to various stimuli and how they map into the brain, we were able to show that the tentacles are exceptionally sensitive touch organs that detect water movements generated by nearby moving objects. That is, the tentacles function exactly as would be expected for a fish-detecting organ in an ambush predator. We also filmed snakes under infrared illumination, which they cannot see, and demonstrated their ability to catch fish without using eyesight. Apparently the tentacles allow snakes to detect and capture fish at night or in murky water. Armed with a world-class motion detector and the ability to scare a target to its death, a tentacled snake is a fish's worst nightmare. SA

MORE TO EXPLORE

Tentacled Snakes Turn C-Starts to Their Advantage and Predict Future Prey Behavior. Kenneth C. Catania in *Proceedings of the National Academy of Sciences USA,* Vol. 106, No. 27, pages 11183–11187; July 7, 2009.

Function of the Appendages in Tentacled Snakes (*Erpeton tentaculatus*). K. C. Catania et al. in *Journal of Experimental Biology,* Vol. 213, No. 3, pages 359–367; February 2010.

Born Knowing: Tentacled Snakes Innately Predict Future Prey Behavior. Kenneth C. Catania in *PLoS ONE,* Vol. 5, No. 6, e10953; June 16, 2010.



World without Fish

by Mark Kurlansky. Illustrated by Frank Stockton.
Workman, 2011 ($16.95)

Tuna, cod, salmon, swordfish—most of the world's commercial fish species may disappear in the next 50 years as a result of overfishing, pollution and global warming. Timed to coincide with Earth Day and the one-year anniversary of the Gulf oil spill, this beautifully illustrated children's book explains how fish came to be so imperiled, how their decline affects other organisms, and what people can do about it.

Cave of Forgotten Dreams

film by Werner Herzog, opens April 29 in theaters across the U.S.

A long time ago, in the dark recesses of a cave in the Ardèche region of south-central France, a visitor working by torchlight expertly applied charcoal to the craggy limestone walls to create a quartet of spirited horses, their mouths open as if whinnying to one another. It is one of humanity's greatest artworks. It is also one of the first: the paintings in this cave known as Chauvet have been dated to around 32,000 years ago, which, if confirmed, would make them the oldest cave paintings on record.

Since the discovery of the cave in 1994, access has been tightly restricted for fear of upsetting the delicate balance of conditions that have preserved the images for millennia; only a handful of people have ever been allowed entry. Luckily for the rest of us, German filmmaker Werner Herzog is one of them, having obtained exclusive permission from the French government to shoot inside the cave.

This 89-minute documentary film represents Herzog's first foray into the 3-D medium. Thanks to this technology, viewers feel the claustrophobia of the initial descent into the cave, followed by the relief of entering the spacious first chamber with its glittering stalactites and stalagmites. But it is the lingering, reverent shots of the paintings—highlighting, for example, the way their creators used the natural contours of the walls to give depth to the creatures they depicted—that most benefit from the 3-D treatment, revealing these Ice Age artists as keen observers of the natural world.

Herzog makes a few missteps, as when he suggests that it is as if the modern human spirit first emerged in western Europe. In fact, mounting evidence, including advanced weaponry and such symbolic items as jewelry, indicates that anatomically modern human beings began thinking like us long before they fanned out from their African birthplace to colonize the rest of the Old World. But that oversight should not deter would-be viewers. Chauvet is a marvel of prehistory, and Herzog's awe-inspiring tour is the closest we will ever get to the real thing.

COMMENT ON THIS ARTICLE ONLINE
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ALSO NOTABLE

Flourish: A Visionary New Understanding of Happiness and Well-being, by Martin Seligman. Free Press, 2011 ($26)

Crashes, Crises, and Calamities: How We Can Use Science to Read the Early-Warning Signs, by Len Fisher. Basic Books, 2011 ($23.99)

Kraken: The Curious, Exciting, and Slightly Disturbing Science of Squid, by Wendy Williams. Abrams, 2011 ($21.95)

Periodic Tales: A Cultural History of the Elements, from Arsenic to Zinc, by Hugh Aldersey-Williams. Ecco, 2011 ($29.99)

The Immortalization Commission: Science and the Strange Quest to Cheat Death, by John Gray. Farrar, Straus and Giroux, 2011 ($24)

Shadows Bright as Glass: The Remarkable Story of One Man's Journey from Brain Trauma to Artistic Triumph, by Amy Ellis Nutt. Free Press, 2011 ($26)

Modernist Cuisine: The Art and Science of Cooking, by Nathan Myhrvold, Chris Young and Maxime Bilet. The Cooking Lab, 2011 ($625)

Infinite Reality: Avatars, Eternal Life, New Worlds, and the Dawn of the Virtual Revolution, by Jim Blascovich and Jeremy Bailenson. William Morrow, 2011 ($27.99)

Inside Jokes: Using Humor to Reverse-Engineer the Mind, by Matthew M. Hurley, Daniel C. Dennett and Reginald B. Adams, Jr. MIT Press, 2011 ($29.95)

First Contact: Scientific Breakthroughs in the Hunt for Life beyond Earth, by Marc Kaufman. Simon & Schuster, 2011 ($26)

FRANK STOCKTON

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Michael Shermer is publisher of *Skeptic* magazine (www.skeptic.com). His next book is *The Believing Brain*. Follow him on Twitter @michaelshermer

UFOs, UAPs and CRAPs

Unidentified Aerial Phenomena offer a lesson on the residue problem in science

One morning several years ago a black triangular-shaped object flew over my home in the San Gabriel Mountains in southern California. It was almost completely silent, made rapid turns and accelerations, and was so nonreflective it looked like a hole in the sky, almost otherworldly. It was, in fact, the B-2 Stealth Bomber, looping around to make another run over the Pasadena Rose Parade on January 1, an annual tradition. But had I not known what it was and seen it first, say, out in the desert at dusk, I might easily have thought it a UFO.

For decades black triangular-shaped objects have been labeled UFOs. Now a cohort of military, aviation and political observers would like to change the label to a less pejorative phrasing—Unidentified Aerial Phenomena (UAP)—and their efforts to be taken seriously have resulted in a new book by investigative journalist Leslie Kean entitled *UFOs: Generals, Pilots, and Government Officials Go on the Record* (Crown, 2010). Kean asks readers to consider that such sightings represent "a solid, physical phenomenon that appears to be under intelligent control and is capable of speeds, maneuverability, and luminosity beyond current known technology," that the "government routinely ignores UFOs and, when pressed, issues false explanations," and that the "hypothesis that UFOs are of extraterrestrial or interdimensional origin is a rational one and must be taken into account."

How much data do we have, and can they help us distinguish between UAPs and what I call Completely Ridiculous Alien Piffle (CRAP), such as crop circles and cattle mutilations, alien abductions and anal probes, and human-alien hybrids? According to Kean, "roughly 90 to 95 percent of UFO sightings *can* be explained" as "weather balloons, flares, sky lanterns, planes flying in formation, secret military aircraft, birds reflecting the sun, planes reflecting the sun, blimps, helicopters, the planet Venus or Mars, meteors or meteorites, space junk, satellites, sundogs, ball lightning, ice crystals, reflected light off clouds, lights on the ground or lights reflected on a cockpit window," and more. So the entire extraterrestrial hypothesis is based on the residue of data after the above list has been exhausted. What's left? Not much.

For example, Kean opens her exploration "on very solid ground, with a Major General's firsthand chronicle of one of the most vivid and well-documented UFO cases ever"—the UFO wave over Belgium in 1989–1990. Here is Major General Wilfried De Brouwer's recounting of the first night of sightings: "Hundreds of people saw a majestic triangular craft with a span of approximately a hundred and twenty feet and powerful beaming spotlights, moving very slowly without making any significant noise but, in several cases, accelerating to very high speeds." Even seemingly unexplainable sightings such as De Brouwer's, however, could simply have been an early experimental model of a stealth bomber (U.S., Soviet, or otherwise) that secret-keeping military agencies were understandably loath to reveal.

In any case, compare De Brouwer's narrative with Kean's summary of the same incident: "Common sense tells us that if a government had developed huge craft that can hover motionless only a few hundred feet up, and then speed off in the blink of an eye—all without making a sound—such technology would have revolutionized both air travel and modern warfare, and probably physics as well." Note how a 120-foot craft becomes "huge," how "moving very slowly" changes to "can hover motionless," how "without making any significant noise" shifts to "without making a sound," and how "accelerating to very high speeds" transforms into "speed off in the blink of an eye." This language transmutation is common in UFO narratives, making it harder for scientists to provide natural explanations.

In all fields of science there is a residue of anomalies unexplained by the dominant theory. That does not mean the prevailing theory is wrong or that alternative theories are right. It just means that more work needs to be done to bring those anomalies into the accepted paradigm. In the meantime, it is okay to live with the uncertainty that not everything has an explanation. SA

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Illustration by Michael Cho

There is one aspect of life that ***unites***, ***controls***, and ***affects*** all people. That one aspect is life's ***natural laws***. They ***unite***, ***control***, and ***affect*** people no matter what their race, gender, creed, or where on this planet they live. Consider that the creator of the laws of physics also created another law to ***unite***, ***control***, and ***affect*** people's relationships with one another.

If you are a new reader of this subject matter, be prepared for a pleasant shock.

Whoever or whatever is the creator revealed nature's law of right action to the mind of Richard W. Wetherill in 1929. The law calls for people to be rational and honest not only regarding the laws of physics but also to be rational and honest in their thinking and behavior toward one another.

After decades of rejection, the behavioral law is as viable and effective as when it was created, whereas people's behavior, in general, has become more and more blatantly irrational and dishonest.

Despite the fact that compliance to each law of physics requires its specific right action in order to succeed, people's behavior toward one another, whether noble or ignoble, was deemed to be a matter of personal choice.

Wetherill used words to describe the elements of nature's law of behavior such as rational, logical, honest, appropriate, moral, and true to the facts. He also cautioned that the law, itself, is the ***final arbiter of right behavior***. The law states: ***Right action gets right results whether it relates to laws of physics or the law of behavior, whereas wrong results in either case indicate the failure to comply.***

There is one requirement of the behavioral law that people need to give careful attention. Rational and honest responses in their relationships with one another must be made specifically to satisfy the law and not to satisfy their particular expectations.

Ordinarily people conduct their relationships to satisfy their purposes, none of which qualify according to natural law. Such behavior, however, does explain why the earth's population is not being peacefully ***united*** and ***controlled*** nor favorably ***affected***.

Do people intentionally refuse to accommodate the requirements of gravity for instance? No, they do their best to keep their balance or recover it when needed.

Behavioral responses require that same attitude. Do not act for personal reasons; act because a self-enforcing, natural law requires people's ***obedience***.

Those who are familiar with the accounts of creation in scriptures will realize that the first wrong act of the created beings was to ***disobey***. That wrong behavior ended the perfect situation that had existed and brought about the predicted wrong results.

Whether those scriptural accounts are actual or symbolic, they graphically illustrate the problem.

For ages people have sought to control their behavior and have suffered myriad troublesome results. Nature's law of behavior when obeyed *unites* people, allowing them to enjoy the benefits that then *control* and favorably *affect* their lives.

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This public-service message is from a self-financed, nonprofit group of former students of Mr. Wetherill.

The ongoing search for fundamental farces

Steve Mirsky has been writing the Anti Gravity column since he was a man trapped in the body of a slightly younger man. He also hosts the *Scientific American* podcast Science Talk.

Killer Entertainment

This may be the golden age of small-screen science

One of the great things about life in 2011 is the technology of television. When I was a kid if you had a Cub Scout meeting when the *Flintstones* was on, you missed the *Flintstones*. Of course, those days are long gone. If you miss a show now, you can watch it later at your leisure on a DVD or via Hulu or iTunes or Amazon or various other ways that violate numerous international copyright laws.

Taking advantage of these new opportunities, I have recently started watching two science-heavy programs of relatively recent vintage: *Dexter* and *Breaking Bad*. Readers who don't know the shows may be driven to try them by what follows. Readers who are up-to-date on the programs should not send me any spoiler information!

Dexter is the story of scientist Vincent Masuka, the lead forensics expert for the Miami Metro Police Department. (The character called Dexter is a lesser forensics worker, who concentrates on blood spatter.) Masuka, who gets little respect from the police he helps, is a generalist well versed in all major forensic techniques.

The series—I'm up to the early episodes of season three—depicts him pursuing his normal job activities but also advancing the entire field of forensics as the sole author of a journal article for the *Forensics Quarterly*. His paper is of such quality that it is accepted and fast-tracked for publication. I can think of no other TV scientist who achieves such a feat.

When the paper is published, Masuka passes out copies to the rest of the police station staff, who ignore it. Masuka even finds a copy in the trash, clearly dumped there by one of his unappreciative colleagues. But the journal article leads to an invite for Masuka to give the keynote address at a forensics conference. He gets tickets for all the cops and other co-workers, but not even his subordinate Dexter is willing to go.

Now, this is going to be some talk. I've gone to many science conference lectures, including one by a sitting president of these United States, and none of them ever required a ticket. Masuka even offers people a free doughnut along with a ticket, but the legendary cop-doughnut affiliation holds no sway. His paper and keynote address will be forgotten.

The disrespect with which Masuka is treated is demonstrated in a meta way by the production of the series itself. Because Masuka actually gets just far less screen time than does Dexter, who, spoiler alert, is also a psychopathic serial killer! The producers thus brilliantly illustrate the scientist, in the person of Masuka, as a modern-day Sisyphus, working tirelessly to advance civilization amid an environment of violence and chaos. Bravo.

I have seen only the first three episodes of *Breaking Bad,* the adventures of a high school chemistry teacher named Walter White. But the series has already featured a wonderful lesson about treating chemicals with respect.

White tells an immature associate to purchase a specific kind of plastic bin, the only kind that will hold hydrofluoric acid safely. White's young charge disregards his instructions and simply pours two large containers of hydrofluoric acid into a bathtub. (The tub holds the remains of a methamphetamine dealer whom White killed. He and the kid are trying to dissolve the body, but never mind that.) The acid eats up most of the contents of the tub, as well as the tub and the floor. When the remains of everything hit one level down, what's left of the acid begins eating away at that floor, too. I would like to see a forensics master like Vince Masuka try to make sense of that scene!

Hydrofluoric acid is in fact incredibly corrosive and dangerous. When I took chemistry in college, we students could pour the hydrochloric or even sulfuric acid with impunity. But we were not even allowed to touch the containers of hydrofluoric. On the rare occasions that we needed it, the lab instructor would don protective gear and pour out a few precious milliliters for us to use under a fume hood.

And so has *Breaking Bad* taken me back to my happy college years and the joy of learning by doing. I can't wait for the next episode. And thanks to modern TV technology, I don't have to. SA

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Illustration by Matt Collins

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April 1961

Tiling

"The Dutch artist Maurits C. Escher, now living in Baarn [near Amsterdam], has applied many of the 17 symmetry groups to mosaics in which animal shapes are used for the fundamental regions. One of Escher's amazing mosaics is reproduced on the cover of this issue of *Scientific American*. Escher is a painter who enjoys playing with mathematical structure. There is a respectable school of aesthetics that views all art as a form of play, and an equally respectable school of mathematics that looks upon all mathematical systems as meaningless games played with symbols according to agreed-upon rules. —Martin Gardner in Mathematical Games"

Economics of Disarmament

"The Federal Government of the U.S. has been spending somewhat more than $40 billion per year on the maintenance of the military establishment and the procurement of arms. These outlays have absorbed about 10 per cent of the gross national product, and they have exceeded by several billion dollars the combined net annual investment in manufacturing, service industries, transportation and agriculture. The negotiation of disarmament would eventually raise the possibility of a substantial cut in the military budget. Economists, market analysts and the makers of fiscal policy in Government and business have therefore begun to consider how the economy might otherwise employ the labor, the plant and the physical resources that now serve—directly and indirectly—the demands of the military establishment. —Wassily W. Leontief and Marvin Hoffenberg"

Leontief was awarded the economics prize from the Nobel Foundation in 1973.

M. C. Escher: the science of symmetry and the mathematics of aesthetics, 1961

April 1911

Race to the South Pole

"Word has been received from Capt. Scott that Amundsen, like himself, is trying to reach the South Pole. Scott's ship, the 'Terra Nova,' has returned to New Zealand after landing sledge parties on the ice, and has brought messages from Capt. Scott himself. It seems that Lieut. Pennell, of the expedition, found the 'Fram,' Amundsen's ship, in Iceland Bay, and a Norwegian party fully equipped for a journey to the South Pole. On board the 'Fram' were eight men and sixteen Greenland dogs. Nothing had been heard of Amundsen's expeditions until news was received from Scott."

Greenwich Time

"On February 10th, 1911, the French Senate passed a bill which makes Greenwich time legal in France. When the law goes into effect, French time will become nine minutes and twenty-one seconds slower than it is now. In order to avoid the expense of altering charts and sailing instructions, the law will not apply to French naval or merchant marine vessels, and it is not likely that any change will be made to the almanacs. French railways are now run by a standard five minutes slower than Paris time, and the clocks inside stations are regulated by this standard, while the clocks on the outside of the station give the correct Paris time. This confusing system will be abolished, and both exterior and interior clocks will be regulated by Greenwich time, by which the trains will be run."

April 1861

Caesium

"The first result of the new method of analysis by the lines of the spectrum was to inform us what substances exist in the sun; the next result is the discovery of two new metals on the earth. One of these has been named caesium, from the color of the peculiar lines in the spectrum of its light; the other is not yet named [later called rubidium]. Caesium resembles potassium in its properties, and exists only in exceedingly small quantities."

Watchmakers

"Frederika Bremer gives the following picture of watchmaking in Geneva: 'The manufacture of pocket-watches is carried to a great extent in Geneva. An immense number are required for the Chinese market. A well-equipped Chinaman, I have been told, carries a watch on each side of his breast, that he may be able to regulate the one by the other. Wealthy Chinese cover the walls of their rooms with watches. These watches are of a more ornamental character, and have more filigree work upon them than those made for Europeans. Long live the Chinese! At one of the greatest and best conducted manufactories of Geneva, nothing but watch faces are prepared, and elderly, well-dressed and well-looking women sat by twenties and thirties in clean, well-warmed rooms, working upon watch faces.' "

The full article by Bremer, a Swedish feminist writer, is available at www.ScientificAmerican.com/apr2011/bremer

SCIENTIFIC AMERICAN, VOL. 204, NO. 4; APRIL 1961

100-Year-Old San Francisco Mint Gold Saved From Destruction

Above: The San Francisco Mint (center) was one of the few buildings left standing after the great earthquake of 1906.

The San Francisco "S" mintmark

Actual size is 21.6 mm

Over a century ago in 1906, San Francisco was devastated by a massive earthquake. On that date the San Francisco Mint forever ceased production of the historic Lady Liberty $5 Half Eagle gold piece. It was the end of an era for the coin that had been made of 90% fine gold with the famous "S" mintmark since the California Gold Rush. Yet for even those coins that survived the calamity of the terrible 1906 earthquake, an even worse fate lay ahead.

Reserved from Massive Meltdown in 1934

In 1934, U.S. gold coins were officially recalled by the Federal Government and melted down into 100-ounce and 400-ounce gold ingots. An estimated 90% of all the San Francisco Liberty $5 gold coins were lost forever.

Surviving "S" Mint Liberty gold coins, few and far between, are increasingly valued by today's collectors. Now, GovMint.com has authorized the limited release of 100-year-old, "S" Mint $5 gold Half Eagles saved from the San Francisco earthquake and subsequent official U.S. Treasury meltdown. These coins are struck in 90% gold and date between1866 and 1906 (date is our choice). They are collector quality, with a numismatic grade of Extremely Fine. During this limited release, you can get these authentic 100 year old gold coins for as little as $650 each (compare with current advertisements from retail coin dealers of up to $799 each).

The History of The West In Your Hands

The history of the American West lives on in these glittering gold coins. The San Francisco Mint was built during the California Gold Rush and minted gold delivered from the miners. San Francisco and the western states grew out of the gold and silver strikes and the immigrants who came from all across the land to build a new future. The images of Miss Liberty and the American Eagle on each U.S. $5 gold coin symbolize our nation's freedom, strength and faith. These precious and enduring coins are becoming more precious and sought-after with each generation and are a valuable legacy for you and your loved ones.

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MONEY-BACK SATISFACTION GUARANTEE

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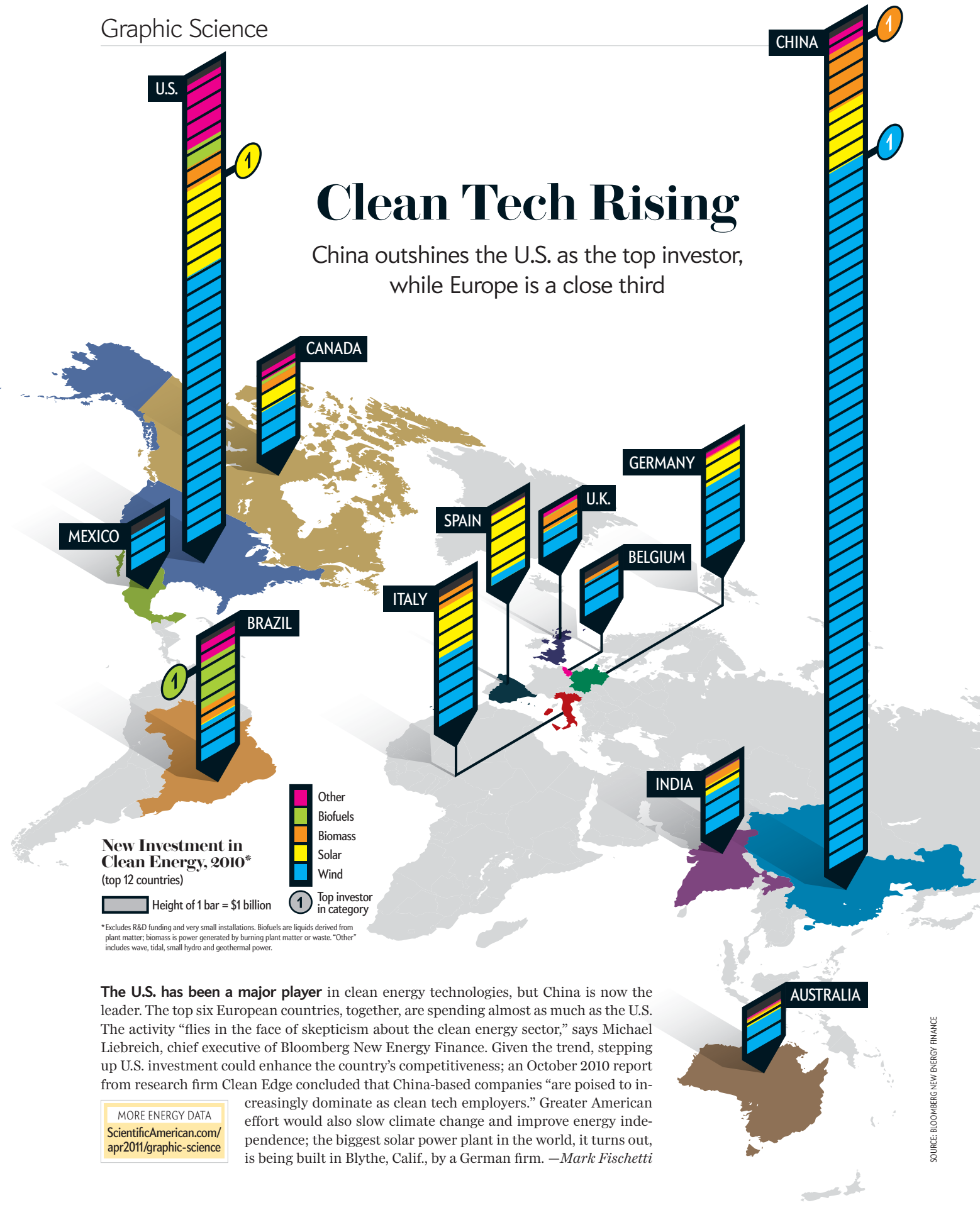
Clean Tech Rising

China outshines the U.S. as the top investor, while Europe is a close third



The U.S. has been a major player in clean energy technologies, but China is now the leader. The top six European countries, together, are spending almost as much as the U.S. The activity "flies in the face of skepticism about the clean energy sector," says Michael Liebreich, chief executive of Bloomberg New Energy Finance. Given the trend, stepping up U.S. investment could enhance the country's competitiveness; an October 2010 report from research firm Clean Edge concluded that China-based companies "are poised to increasingly dominate as clean tech employers." Greater American effort would also slow climate change and improve energy independence; the biggest solar power plant in the world, it turns out, is being built in Blythe, Calif., by a German firm. —*Mark Fischetti*

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