NEUROSCIENCE
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May 2012

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A Unified Physics?

New Efforts to Unite Quantum Mechanics with Einstein's Relativity

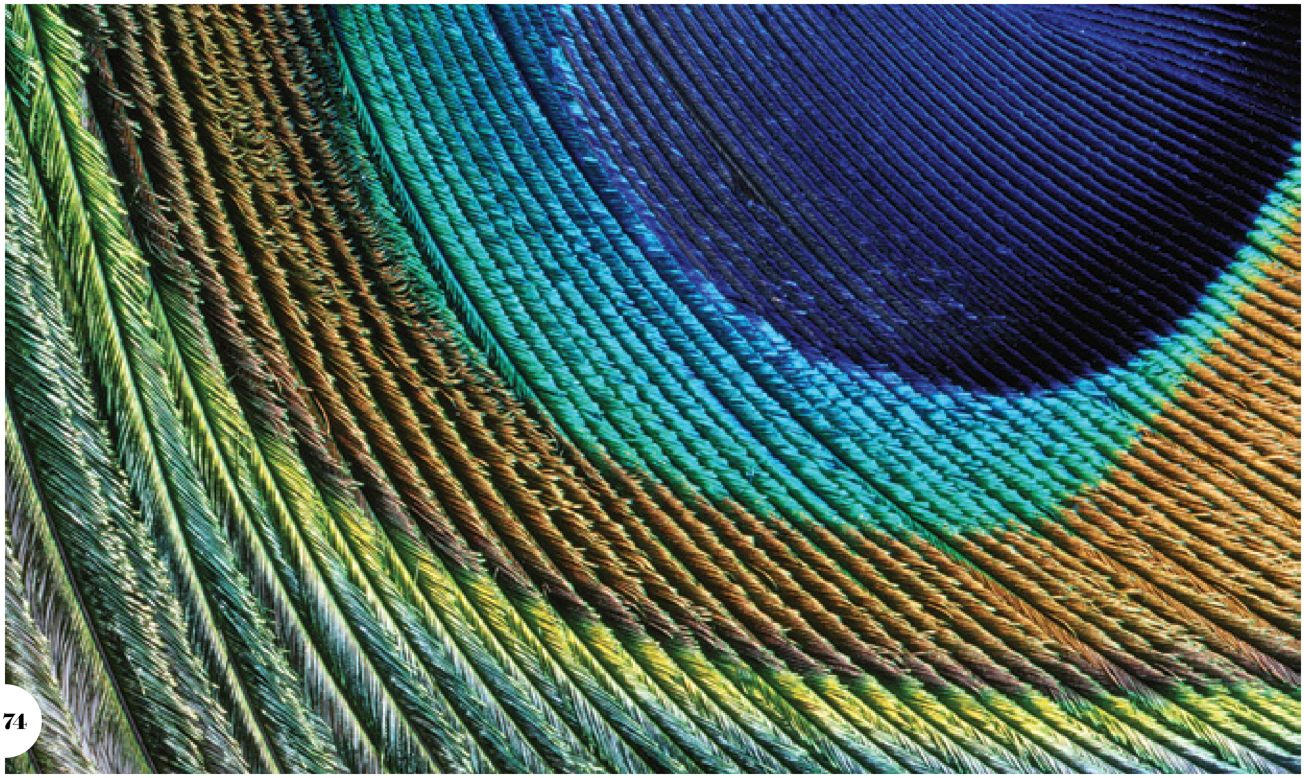
SPECIAL REPORT
YOUR FUTURE HEALTH

SCIENTIFIC AMERICAN

May 2012 Volume 306, Number 5

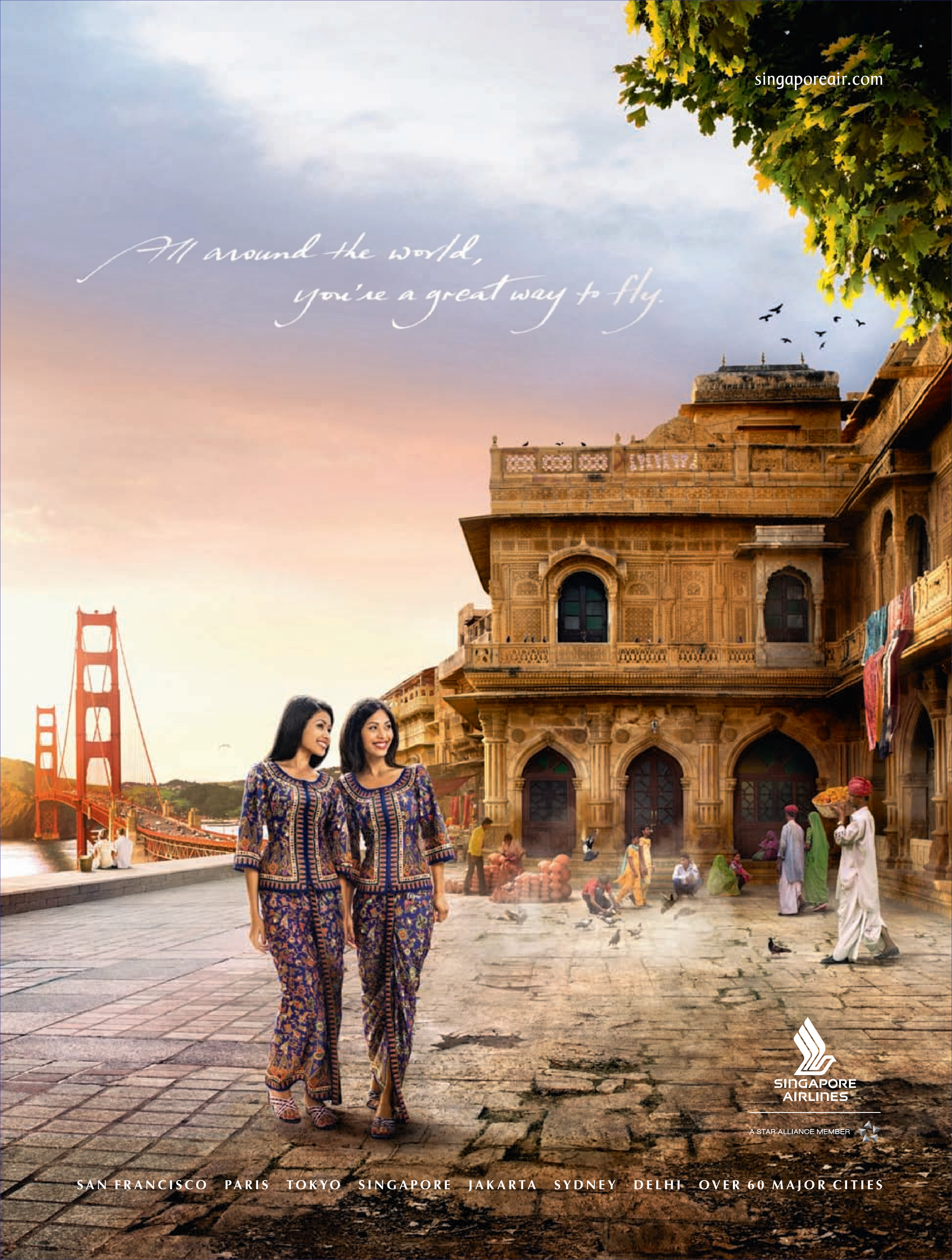
ON THE COVER

Particle physicists have been stymied by the complexity of their theories, which are commonly expressed in terms of stylized diagrams developed by the bongo-drumming Nobelist physicist Richard Feynman. A fresh approach breaks the calculational logjam and solves problems once thought beyond mortal minds, possibly including the unification of physics. Image by Kenn Brown, Mondolithic Studios.



DARRELL GULIN *Getty Images (peacock feather detail)*

FEATURES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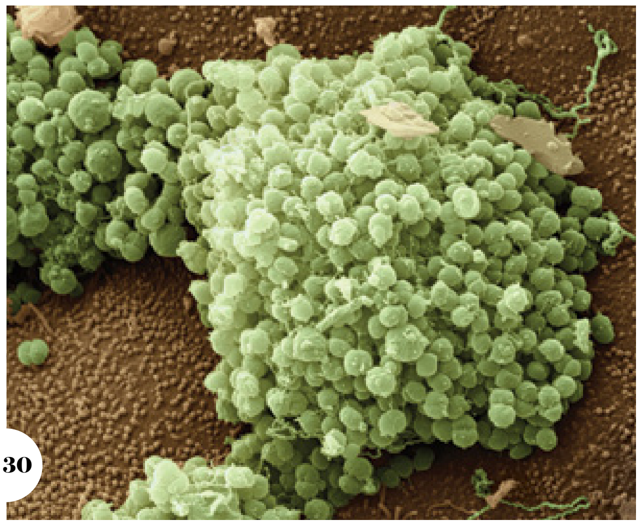

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DEPARTMENTS

ON THE WEB

Moon and Mercury and Mars—Oh, My!
At the 43rd Lunar and Planetary Science Conference in Texas, researchers shared the latest findings on the moon's early years, pored over the most detailed images ever taken of Mercury and Mars, and examined the 50-year history of nuclear power in space.
Go to www.ScientificAmerican.com/may2012/planets

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It's a typically sunny day in MacArthur Park. The kids are playing tag. A new mom is pushing a stroller. Senior citizens are doing tai chi.

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

New Physics and Future Medicine

PHYSICISTS HAVE BEEN STRUGGLING FOR DECADES to unify quantum mechanics, which corrals the particle flock, with Einstein's general theory of relativity, which sculpts space and time. They've come at it with various approaches, including string theory, but it remains stubbornly intractable. Yet—taking a common tactic that physicists use to break apart complex challenges—what if we simplified the problem?

They've now come to a whole new understanding of quantum particles that enormously eases the task. A hypothetical particle, the "graviton," shapes spacetime, bringing unity to the two theories at last. For a fascinating armchair journey through a different kind of spacetime, turn to page 34 for this issue's cover story, "Loops, Trees and the Search for New Physics," by Zvi Bern, Lance J. Dixon and David A. Kosower.

Among earthly concerns, maintaining health ranks high for most of us. Our special report, "Tomorrow's Medicine," starting on page 42, will give you a view of what's next. You will learn how nanoparticles could help detect cancer earlier, when it is easiest to eliminate; how smart implantable devices could warn of an imminent heart attack or help manage diabetes; how retinal chips and synthetic photoreceptors could restore sight; and how personalized medicine may finally arrive. As always, we welcome your feedback. SA

SCIENCE IN ACTION

Meet the *Scientific American* Imprint

It's been many years, of course, since *Scientific American* was "just" a magazine (and, for those who don't know, it is the longest continuously published magazine in the U.S. at that). In addition to the monthly print glossy, you can get regular updates from our staff and bloggers online at www.ScientificAmerican.com on your mobile phone and, soon, in regular tablet apps. But this month I wanted to focus on the newest member of the *Scientific American* editorial family—a book imprint developed with our sister company Farrar, Straus and Giroux (FSG).

For many months I have been working closely with Amanda Moon of FSG, who is spearheading the effort to find the best, most authoritative voices for the imprint. She has attended our editorial board meetings, visited conferences and otherwise canvassed the research world for authors who can provide the kinds of in-depth, scientifically compelling books that you would expect from *Scientific American.* "What a Plant Smells," by Daniel Chamovitz, starting on page 62, is the first excerpt in a series that we will run as the books become available; more materials, including blogs by the authors, will appear on our site.

The books join the first imprint title, the acclaimed Journey to the Exoplanets iPad app created by former longtime *Scientific American* art director Edward Bell and Hugo Award–winning artist Ron Miller. Enjoy! —*M.D.*

Illustration by Nick Higgins


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editors@sciam.com

January 2012

SCREENING STATS

During my 30-year practice of diagnostic radiology, I spent many hours educating physicians and surgeons on the importance of false positives and false negatives in the diagnostic process. No diagnostic test is 100 percent accurate. My mantra was always: don't treat initial test results. Always confirm the diagnosis with other independent data before performing surgery or prescribing pharmaceuticals with serious side effects.

I applaud the general theme of mathematician John Allen Paulos in "Weighing the Positives" [Advances]. First he makes the valid argument that medical tests will be positive for some patients without disease. He then illustrates this with a statistical analysis of mammography on one million patients, resulting in 9,960 false positives. He makes a monumental error, however, in stating, "If the 9,960 healthy people are subjected to harmful treatments ranging from surgery to chemotherapy to radiation, the net benefit of the tests might very well be negative."

Because mammography, prostate-specific antigen levels and all other initial testing for common cancers are merely screening tests, no patient ever receives definitive treatment for cancer before these tests are confirmed by a biopsy. Cynical health care watchdogs may cite this as excessive testing, but such measures avoid the negative effects of overtreatment that Paulos invokes.

J. G. McCully
via e-mail

"If the initial bias in predictive policing is for factors other than crime, the result may be the deepening of injustice."
MICHAEL JACOB *VIA E-MAIL*

PREDICTIVE PREJUDICE

In "The Department of Pre-Crime," James Vlahos mentions the potential danger of prejudging individuals by using predictive policing techniques but avoids discussion of a more serious potential consequence of such "crime forecasting": the positive-feedback reinforcement of existing biases to more deeply criminalize certain populations and deepen injustice.

If police are already focusing on and arresting in some neighborhoods over others, feeding information into the machine may result in still greater police presence, more arrests, more predicted crime, still more police presence and still more arrests. If the initial bias is for factors other than actual crime, the result may be the deepening of injustice, not a reduction of crime.

The racial, ethnic and financial divides in crime and justice in the U.S. are well documented. The most obvious examples are in the discrepancies in drug laws, where the use of "crack" cocaine gets far more serious penalties than the powdered version, with the meaningful difference being that crack is used primarily in black communities.

African-Americans are perhaps eight times more likely to be incarcerated than whites. Poor people are much more likely to be convicted and sent to prison than wealthier people. Young people in poorer, nonwhite neighborhoods have a much different experience with respect to the police than whites. They are probably more likely to get a criminal record than their white counterparts in wealthier communities who engage in the same behaviors.

Once into the criminal system, people can lose their right to vote, have their reputations and futures tainted, and have reduced access to jobs. They are, in a sense, trained to continue and pass on a more criminal culture.

Michael Jacob
via e-mail

OVERRATED DOWN UNDER?

Although the gist of the "The Coming Mega Drought" [Forum]—Peter H. Gleick and Matthew Heberger's essay on the possibility of Australia's Millennium Drought being repeated in the southwestern U.S.—rings true, the comments praising Australia's response to its drought need a bit of context. There is unfortunately a political aversion to human reuse of water in Australia. (I have heard a specific put-down: "Would you like to drink poo water?") The $13.2 billion being spent by the country's five largest cities to add to desalination capacity is extremely wasteful as the same end can possibly be achieved by treatment and reuse. Desalination is also energy-intensive.

James Fradgley
Wimborne, England

Much of Australia's response to the Millennium Drought has been good, but some of it has been disastrously wasteful. Victoria's previous state government, for instance, spent megadollars on a pipeline, now mothballed, to take water from agricultural irrigation land north of the Great Dividing Range so as to ensure Melbourne had water to flush down its toilets. And the cost of desalination is arguably unnecessary when subsidizing the harvesting of roof runoff was apparently not even considered.

The U.S. could learn from some of our water-saving efforts—but not all of them!

Les G. Thompson
Victoria, Australia.

HEBERGER REPLIES: Both letters raise valid and interesting points. There was no room to delve into these issues in the short space available. For a more detailed review of these issues, please see Chapter 5

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(*"Australia's Millennium Drought: Impacts and Responses") in* The World's Water, *Vol. 7, edited by Peter H. Gleick (Island Press, 2011).*

INTELLIGENCE OPTIONS

Michael Shermer's "In the Year 9595" [Skeptic] confuses different aspects of computer intelligence: emergence of computers that can be called intelligent or conscious (two different milestones); the "singularity" (in which a replicator starts creating generations of capability faster than humans can comprehend); and transference of a human into a different "container."

Shermer assumes that computer intelligence will emerge because we design a computer to accomplish that. But other paths include creating learning machines that develop intelligence or consciousness from this activity, as in the human brain. Or some tipping point may occur within the complexity of computers, networks and other technology. We need not understand what will result from our creations.

I anticipate computers that can pass the Turing test of consciousness [in which answers to questions cannot be distinguished from answers a human gives] by midcentury and devices that assert their own consciousness by the end of the century. John Brunner's supercomputer in the 1968 novel *Stand on Zanzibar* responded to the question "Are you or aren't you a conscious entity?" with: "It appears impossible for you to determine if the answer I give to that question is true or false." I suspect Brunner's computer is correct.

There are again multiple paths to singularity. Once we have silicon devices that reproduce silicon devices somewhat autonomously, one route is established. Genetic engineering of people could also lead in this direction, as could cyborg approaches.

On transferring personality to another platform, I agree with Shermer's skepticism. It is marginally conceivable that a "clone" might be able to receive a brain transplant. But it is very likely we will have intelligent machines before we have a platform that can adopt sufficient aspects of human personality, and once we have machines that intelligent, why would they support this activity?

Jim Isaak
Bedford, N.H.

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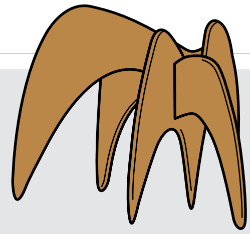

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LETTERS TO THE EDITOR

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Letters may be edited for length and clarity. We regret that we cannot answer each one. Post a comment on any article at ScientificAmerican.com/may2012

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Fresh Fruit, Hold the Insulin

While health officials wage a costly war on obesity and diabetes, taxpayers are subsidizing foods that make us fatter. It's time to rewrite the farm bill

PIOTR POWIETRZYNSKI *Getty Images*

Some years ago two nutrition experts went grocery shopping. For a dollar, Adam Drewnowski and S. E. Specter could purchase 1,200 calories of potato chips or cookies or just 250 calories worth of carrots. It was merely one example of how an unhealthy diet is cheaper than a healthy one. This price difference did not spring into existence by force of any natural laws but largely because of antiquated agricultural policies. Public money is working at cross-purposes: backing an overabundance of unhealthful calories that are flooding our supermarkets and restaurants, while also battling obesity and the myriad illnesses that go with it. It is time to align our farm policies with our health policies.

In past years farm subsidies have been a third rail of American politics—never to be touched. But their price tag, both direct and indirect, has now brought them back into the debate and created an imperative for change. Conditions such as heart disease, diabetes and arthritis are strongly correlated with excess poundage and run up medical bills of nearly $150 billion every year. The government has poured billions of dollars into dietary campaigns, from the U.S. Department of Agriculture's new MyPlate recommendation (half of daily food consumption should be fruits and vegetables) to programs aimed at providing more produce in schools and in military cafeterias.

Agricultural subsidies undercut those efforts by skewing the market in favor of unhealthful calories. Much of the food we have to choose from—and how much it costs—is determined by the 1,770-page, almost $300-billion Food, Conservation, and Energy Act of 2008 (commonly known as the "farm bill"). This piece of legislation, up for renewal this year, covers everything from nutrition assistance programs to land conservation efforts. It also determines how much money gets paid out to agricultural operations in subsidies and crop insurance programs. Federal support for agriculture, begun in earnest during the Great Depression, was originally intended as a temporary lifeline to farmers, paying them extra when crop prices were low. Nearly eight decades later the benefits flow primarily to large commodity producers of corn and soy, which are as profitable as ever.

The current bill gives some $4.9 billion a year in automatic payments to growers of such commodity crops, thus driving down prices for corn, corn-based products and corn-fed meats. Cows that are raised on corn, rather than grass, make meat that is higher in calories and contains more omega-6 fatty acids and fewer omega-3 fatty acids—a dangerous ratio that has been linked to heart disease.

Cheap corn has also become a staple in highly processed foods, from sweetened breakfast cereals to soft drinks, that have been linked to an increase in the rate of type 2 diabetes, a condition that currently affects more than one in 12 American adults. Between 1985 and 2010 the price of beverages sweetened with high-fructose corn syrup dropped 24 percent, and by 2006 American children consumed an extra 130 calories a day from these beverages. Over the same period the price of fresh fruits and vegetables rose 39 percent. For families on a budget, the price difference can be decisive in their food choices.

But fruits and vegetables do not have to be more expensive than a corn-laden chicken nugget or corn syrup–sweetened drink. One reason they are costly is that the current farm bill categorizes them as "specialty crops" that do not receive the same direct payments or crop insurance that commodity crops do.

With the government tightening its belt, some of those old subsidies finally look ready to fall. Many lawmakers across the political spectrum, including President Barack Obama and the leaders of the U.S. Senate Committee on Agriculture, Nutrition and Forestry, have recommended cutting direct commodity payments, which would save money and help us stay healthier.

There is no dearth of policy options. Research groups such as the Robert Wood Johnson Foundation in Princeton, N.J., recommend leveling the playing field by extending subsidies and insurance programs more widely to fruit and vegetable producers. The government can also use its own purchasing power, through school lunch programs and institutional buying decisions, to fill people's plates with healthy choices. The imperative, however, is clear: any new farm bill should at the very least remove the current perverse incentives for people to eat unhealthily. ■

SCIENTIFIC AMERICAN ONLINE
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Commentary on science in the news from the experts

Alice P. Gast is president of Lehigh University.

Boundary Conditions

A Mexican, a German and an American were working in a physics lab ...

Nations are rivals in soccer and international relations, but science is a unifying force. Many of our biggest achievements seem to come from international collaborations. A team from 11 laboratories in nine countries identified the SARS coronavirus in 2003 with unprecedented speed. Scientists come from all over to chase the Higgs boson at the Large Hadron Collider near Geneva. Centers of excellence dot the globe. The world of science is getting flatter.

What has gone underappreciated in this trend is the effect on science itself and how science is actually done. It has become a cliché that great discoveries come from interdisciplinary thinking—a chemist bringing insight to a discussion of a materials problem, a physicist sharing an intuition about a problem in biology, a biologist helping an engineer see how nature comes up with optimal solutions. Few realize how much science is energized when team members have different cultural approaches to problem solving. International diversity is just as important as diversity of discipline.

I have seen this phenomenon at close quarters. For years I have collaborated with colleagues from Mexico and Germany. We see eye to eye on so many things. We like one another's cuisine, hiking, and the mathematics and physics our research involves. When we began writing out equations on a chalkboard, though, our cultural differences became apparent.

When we first started out, our approaches seemed irreconcilable. The physics problems we work on—fluid suspensions of small particles—are hard. They encompass many unknowns, and the physics bumps up against many constraints and boundary conditions—rules that cannot be broken, like conservation of matter or the impassibility of a solid wall. While working on difficult equations, my Mexican cohorts wanted to relax the rules to make the mathematics more tractable and later put them back in. This set our German friends on edge. They kept reminding us of the constraints and the boundary conditions to make sure we did not stray too far. My American training left me somewhere in the middle: I worried about the constraints but was tentatively willing to relax them.

Over the years the creative clash of viewpoints bred success. The German-Mexican teams, along with some Americans, wound up solving challenging multibody hydrodynamics problems—the complicated mathematical descriptions of the way swarms of particles squeeze the fluid between them, explaining the flow behavior of pastes and slurries.

I first got a lesson in cross-cultural dynamics during a NATO postdoctoral fellowship in Paris in 1985. Working with French colleagues taught me a different way to simplify and clarify a physics problem. An appreciation for the beauty of the problem and the value of intuition might have led us to solutions more easily than the typical American approach: to attack the problem with loads of mathematical equations. Later in Germany, as an Alexander von Humboldt Foundation awardee, I found that approaching an experimental problem with a deliberate, tactical and strategic way reduced the need for trial and error.

The power of this diversity of thought comes alive in international conferences where there is an opportunity to listen, ask questions, think about problems, confer with and critique one another, and continue the dialogue after the meeting is over.

New institutions have sprung up to take advantage of the synergies in multinational collaborations. Singapore has created an intensely international science scene, where talent converges to contribute and compete to form some of the best research teams in the world. In December, King Abdullah University of Science and Technology graduated its second cohort of men and women receiving master's degrees in science and engineering, who hail from Saudi Arabia, China, Mexico, the U.S. and 29 other countries. Labs, institutes and universities are hubs that gather the best scientists to tackle the hardest problems.

The need to reach across national boundaries places greater demands on scientists. While scientists become more specialized as they proceed through their studies, broadening and collaborative experiences make them better able to "think differently" and "connect the dots" to discover new things. Ultimately it leads to better science. SA

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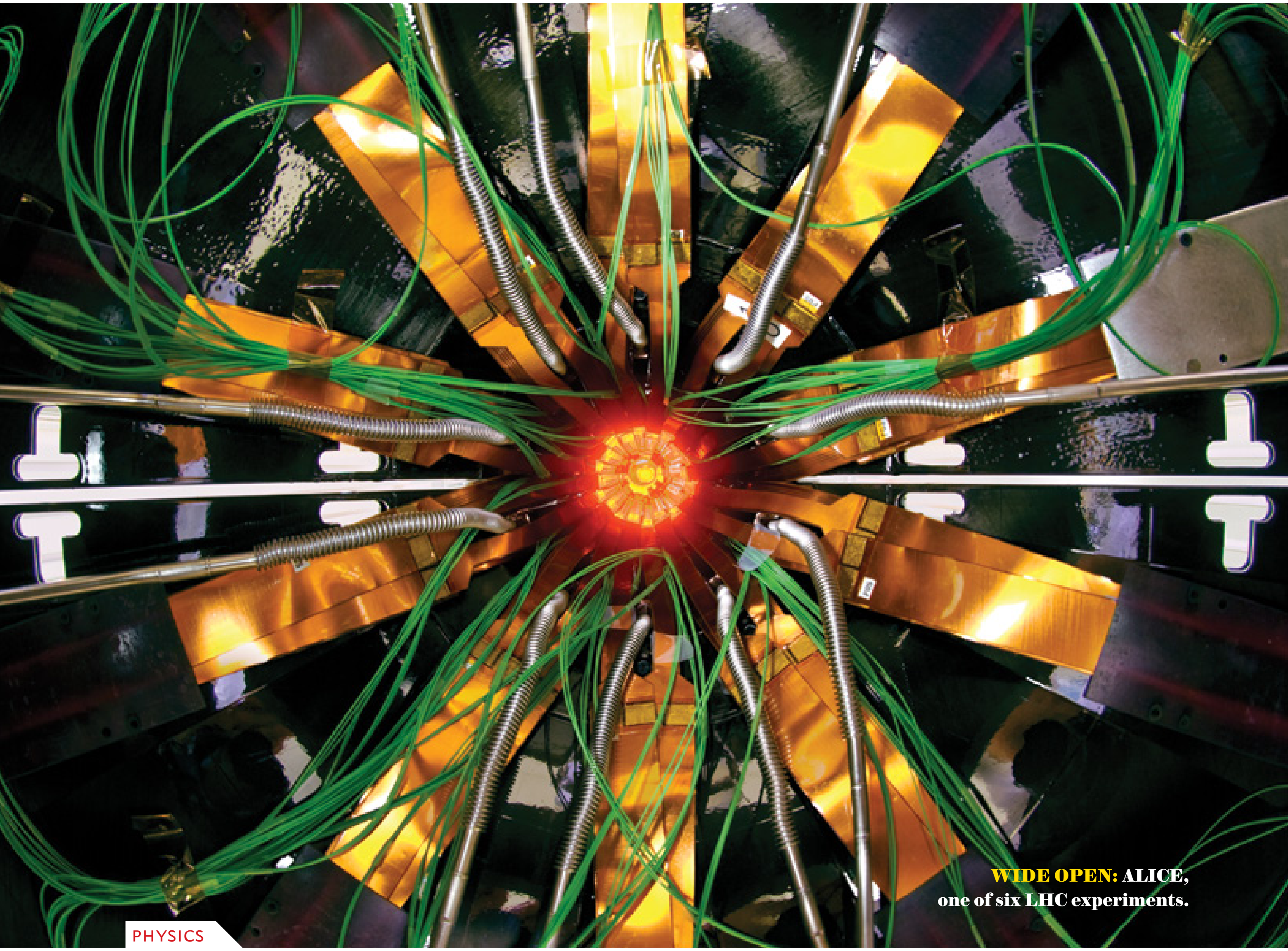
Illustration by Oliver Munday and Jason Arias

ADVANCES

Dispatches from the frontiers of science, technology and medicine



WIDE OPEN: ALICE, one of six LHC experiments.

PHYSICS

Is Supersymmetry Dead?

The grand scheme, a stepping-stone to string theory, is still high on physicists' wish lists. But if no solid evidence surfaces soon, it could begin to have a serious PR problem

For decades now physicists have contemplated the idea of an entire shadow world of elementary particles, called supersymmetry. It would elegantly solve mysteries that the current Standard Model of particle physics leaves unexplained, such as what cosmic dark matter is. Now some are starting to wonder. The most powerful collider in history, the Large Hadron Collider (LHC), has yet to see any new phenomena that would betray an unseen level of reality. Although the search has only just begun, it has made some theorists ask what physics might be like if supersymmetry is not true after all.

"Wherever we look, we see nothing—that is, we see no deviations from the Standard Model," says Giacomo Polesello of Italy's National Institute of Nuclear Physics in Pavia. Polesello is a leading member of the 3,000-strong international collaboration that built and operates ATLAS, one of two cathedral-size general-purpose detectors on the LHC ring. The other such detector, CMS, has seen nothing, either, according to an update presented at a conference in the Italian Alps in March.

Theorists introduced supersymmetry in the 1960s to connect the two basic types of particles seen in nature, called fermions and bosons. Roughly speaking, fermions are the constituents of matter (the electron being the quintessential

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example), whereas bosons are the carriers of the fundamental forces (the photon in the case of electromagnetism). Supersymmetry would give every known boson a heavy "superpartner" that is a fermion and every known fermion a heavy partner that is a boson. "It is the next step up toward the ultimate view of the world, where we make everything symmetric and beautiful," says Michael Peskin, a theorist at SLAC National Accelerator Laboratory.

The monumental collider at CERN near Geneva should have the oomph to produce those superparticles. Currently the LHC is smashing protons with an energy of four trillion electron volts (TeV) apiece, up from 3.5 TeV last year. This energy is divided among the quarks and gluons that make up the protons, so the collision can generate new particles with the equivalent of about 1 TeV of mass. But despite the high expectations (and energies), so far nature has not cooperated. LHC physicists have been searching for signs of particles new to science and have seen none. If superparticles exist, they must be even heavier than many physicists had hoped. "To put it bluntly," Polesello says, "the situation is that we have ruled out a number of 'easy' models that should have showed up right away." His colleague Ian Hinchliffe of Lawrence Berkeley National Laboratory echoes him: "If you look at the range of masses and particles that have been excluded, it's quite impressive."

Many are still hopeful. "There are still very viable ways of building supersymmetry models," Peskin says. Expecting to see new physics after just a year of data taking was unrealistic, says Joseph Lykken, a theorist on the CMS team.

What has theorists on edge, however, is that for supersymmetry to solve the problems for which it was invented in the first place, at least a few of the superparticles should not be too heavy. To constitute dark matter, for example, they need to weigh no more than a few tenths of 1 TeV.

Another reason most physicists want some superparticles to be light lies in the Higgs boson, another major target of the LHC. All elementary particles that have mass are supposed to get it through their interaction with this boson and, secondarily, with a halo of fleeting "virtual particles." In most cases, the symmetries of the Standard Model ensure that these virtual particles cancel one another out, so they contribute only modestly to mass. The exception, ironically, is the Higgs itself. Calculations based on the Standard Model yield the paradoxical result that the boson's mass should be infinite. Superpartners would solve this mystery by providing greater scope for cancellations. A Higgs mass of around 0.125 TeV, as suggested by preliminary results announced in December 2011, would be right in the range where supersymmetry predicts it should be. But in that case, the superparticles would need to have a fairly low mass.

If that proves not to be the case, one explanation is that heretofore underappreciated symmetries of the Standard Model keep the Higgs mass finite, as Bryan Lynn of University College London suggested last year. Others say Lynn's idea would provide at best a partial explanation, leaving a vital role for physics beyond the Standard Model—if not supersymmetry, then one of the other strategies that theorists have devised. A popular plan B is that the Higgs boson is not an elementary particle but a composite of other particles, just as protons are composites of quarks. Unfortunately, the LHC simply does not have enough data to say much about that idea yet, says CERN's Christophe Grojean. More exotic options, such as extra dimensions of space beyond the usual three, may forever lie beyond the LHC's reach. "Right now," points out Gian Francesco Giudice, another theorist at CERN, "every single theory has its own problems."

> ***"There are still very viable ways of building supersymmetry models," says one theorist working on the problem.***

As ATLAS and CMS continue to accumulate data, they will either discover superparticles or exclude wider ranges of possible masses. Although they may never be able to strictly disprove supersymmetry, if the collider fails to find it, the theory's usefulness may fade away, and even its most hardcore supporters may lose interest. That would be a blow not just to supersymmetry but also to even more ambitious unified theories of physics that presume it, which include string theory and other approaches [see "Loops, Trees and the Search for New Physics," by Zvi Bern, Lance J. Dixon and David A. Kosower, on page 34]. LHC physicists take this uncertainty in stride and expect the collider to find some new and exciting physics—not just the physics theorists had expected. Hinchliffe says, "The most interesting thing we will see is something that nobody thought of."

—Davide Castelvecchi

COMMENT AT ScientificAmerican.com/may2012

ECOLOGY

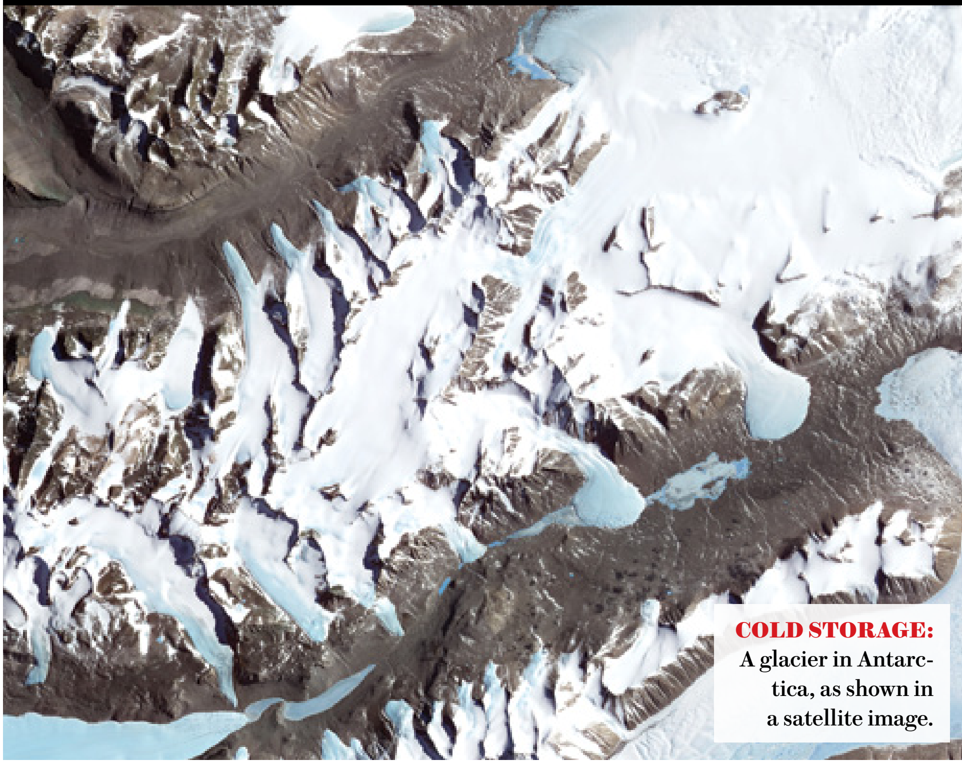
Bright Microbes

Scientists uncover new clues to bioluminescence

Bioluminescent bays are among the rarest and most fragile of ecosystems. They form when large numbers of microorganisms, often dinoflagellates such as *Pyrodinium bahamense,* congregate in a lagoon with an opening narrow enough to keep the organisms from escaping. The dinoflagellates feed on vitamin B_{12} produced by red mangrove trees and glow bluish-green when disturbed by motion of any kind, although scientists have yet to fully understand the phenomenon. Because "bio bays" need very specific conditions to survive, there are only a handful worldwide, and most of the known ones are in the Caribbean.

In 2010 ecologists identified a new bio bay in Puerto Rico's Humacao Natural Reserve and are studying it for clues to how best to preserve these ecosystems. The Humacao bio bay formed after the U.S. Army Corps of Engineers built channels to protect nearby towns from flooding. The channels allowed saltwater from the Caribbean to flow into once brackish Humacao lagoons. "Along with the tide, in came a bioluminescent dinoflagellate," says Ricardo Colón-Rivera, an ecology graduate student at Texas A&M University.

Colón-Rivera and his colleagues have found, to their surprise, that the dinoflagellate responsible for the light show may not be *P. bahamense* but another organism they have yet to identify. They are also hoping to understand the effects of salinity, rainfall and climate change on bioluminescence so they can help preserve bio bays like the one at Humacao. The Humacao bay came to life "because of a confluence of very unusual events," says Rusty Feagin, a coastal ecologist at Texas A&M. "We need to understand and protect it—before its lights go out." —*Cheryl Lyn Dybas*



COLD STORAGE: A glacier in Antarctica, as shown in a satellite image.

CREATED BY JESSE ALLEN, USING DATA PROVIDED COURTESY OF NASA/GSFC/METI/ERSDAC/JAROS AND U.S./JAPAN ASTER SCIENCE TEAM

MICROBIOLOGY

Bugs in the Ice Sheet

Melting glaciers could liberate ancient microbes

Locked in frozen vaults in Antarctica and Greenland, a lost world of ancient creatures awaits another chance at life. Once thought to be too harsh and inhospitable to support any living thing, the polar ice sheets are now known to be a gigantic reservoir of microbial life, trapped longer than modern humans have walked the planet.

With that ice melting at an alarming rate, the earth could soon see masses of bacteria and other microbes the likes of which it has not seen since the Middle Pleistocene, a previous period of major climate change, some 750,000 years ago.

John Priscu, a microbial ecologist at Montana State University, has spent the past 28 austral summers in Antarctica, studying what he calls "the bugs in the ice sheet." He has found living bacteria in cores of 420,000-year-old ice that are still able to grow and divide.

Do they pose a threat to human health? Not likely, scientists say, because most of what has been identified appears related to common soil and marine bacteria. Still, with heat-trapping greenhouse gases warming the polar regions much faster than the rest of the planet today, investigators have many other questions about these organisms.

Researchers are trying to determine how they can sit in a state of suspended animation for millennia. The findings could point the way for the discovery of life in other extreme climates, such as frozen planets and moons.

But the more immediate concerns sit here on earth. Cells and carbon dumped out of melting glaciers could turn into huge piles of decomposing organic matter that generate carbon dioxide and methane as they decay, a potentially significant source of greenhouse gas emissions that climate researchers have yet to consider. And scientists see evidence that the microbes are evolving inside the ice sheets, exchanging DNA and gaining new traits that could let them take over ecological niches.

Although these cold-loving organisms do not appear to endanger the existence of warm-blooded creatures, they could force out existing microbial populations, with unknown consequences.

—Cheryl Katz

Katz is a writer for the news service DailyClimate.org.

SCIENCE PRIZES

In an effort to spur big science discoveries, the U.S. government and private groups have started offering cash prizes. Some examples:

$25 MILLION	$10 MILLION	$2 MILLION	$1.5 MILLION	$1.35 MILLION	$1 MILLION
Name: Virgin Earth Challenge	**Name:** NewOrgan Prize	**Name:** DARPA Urban Challenge	**Name:** Sample Return Robot Challenge	**Name:** Green Flight Challenge	**Name:** PETA prize
Goal: A system that can remove greenhouse gases from the air for 10 years or more and that is eco-friendly.	**Goal:** To use regenerative medicine to grow a new organ and to transplant that organ into a patient and have it function for at least two years by 2020.	**Goal:** Develop and drive fully autonomous vehicles in a long-distance competition. (It was awarded in 2007.)	**Goal:** Build a rough-terrain robot capable of finding and retrieving geologic samples.	**Goal:** Build an aircraft that can fly 200 miles on a gallon of gasoline per passenger. (It was awarded in 2011.)	**Goal:** Develop a way to grow and manufacture in vitro chicken meat that tastes just like real chicken.
From: Al Gore and Richard Branson	**From:** Methuselah Foundation	**From:** Department of Defense	**From:** NASA and Worcester Polytechnic Institute	**From:** NASA, CAFE Foundation and Google	**From:** People for the Ethical Treatment of Animals

COMMENT AT ScientificAmerican.com/may2012

BLAINE HARRINGTON III *Corbis*

MEDICINE

Weighing the Risks

Women who opt for epidurals are more likely to run a fever during labor that can endanger their baby

One of the biggest choices an expectant mother faces is how to handle the pain of childbirth. More than 60 percent of American women choose relief in the form of an epidural, a combination of local anesthetic and narcotic administered into the epidural space surrounding the spinal cord. Although most doctors believe that the injections are safe, a new study suggests that they may increase the risk that a mother will develop a fever during labor, which could, in rare instances, pose risks to her baby.

Epidurals have long been controversial. Some studies have suggested that women who ask for them are more likely to have emergency cesarean sections, but a 2011 review reported that epidurals do not increase C-section risk compared with other forms of pain relief. The same study did find, however, that epidurals make it more likely that doctors will have to deliver with the help of forceps or a vacuum.

Now mothers have new findings to factor into their decisions. In a study published in February in the journal *Pediatrics,* researchers at the Harvard School of Public Health and Harvard Medical School followed 3,209 women with low-risk pregnancies who were giving birth to their first child. Of those receiving epidurals, nearly one out of five developed a fever of at least 100.4 degrees Fahrenheit during labor compared with only 2.4 percent of those receiving other drugs or no pain relief. The higher the mother's fever, the more likely the baby was to have low Apgar scores after birth—an indicator of overall newborn health—as well as low muscle tone and breathing difficulties. And the 8.6 percent of women receiving epidurals who developed a fever of greater than 101 degrees F were more than six times as likely as nonfebrile moms to have babies who had newborn seizures, although the overall seizure risk was only 1.3 percent. No one knows why epidurals appear to be associated with fevers, but senior author Ellice Lieberman, a biologist and obstetrician at the Harvard School of Public Health, believes that the drugs might be invoking an inflammatory response.

The big remaining question is whether these fevers might have more permanent health effects. "We don't really know," Lieberman says, but most effects "seem to be transient." Nevertheless, because a fever takes an average of six hours to develop after an epidural has been administered, women who want to minimize their risk could consider asking for pain relief only when baby seems well on its way.

—Melinda Wenner Moyer

COMMENT AT ScientificAmerican.com/may2012

DO THE MATH

Goldbach's Prime Numbers

A centuries-old conjecture is nearing its solution

One of the oldest unsolved problems in mathematics is also among the easiest to grasp. The weak Goldbach conjecture says that you can break up any odd number into the sum of, at most, three prime numbers (numbers that cannot be evenly divided by any other number except themselves or 1). For example:

$$35 = 19 + 13 + 3$$

or

$$77 = 53 + 13 + 11$$

Mathematician Terence Tao of the University of California, Los Angeles, has now inched toward a proof. He has shown that one can write odd numbers as sums of, at most, five primes—and he is hopeful about getting that down to three. Besides the sheer thrill of cracking a nut that has eluded some of the best minds in mathematics for nearly three centuries, Tao says, reaching that coveted goal might lead mathematicians to ideas useful in real life—for example, for encrypting sensitive data.

The weak Goldbach conjecture was proposed by 18th-century mathematician Christian Goldbach. It is the sibling of a statement concerning even numbers, named the strong Goldbach conjecture but actually made by his colleague, mathematician Leonhard Euler. The strong version says that every even number larger than 2 is the sum of *two* primes. As its name implies, the weak version would follow if the strong were true: to write an odd number as a sum of three primes, it would be sufficient to subtract 3 from it and apply the strong version to the resulting even number.

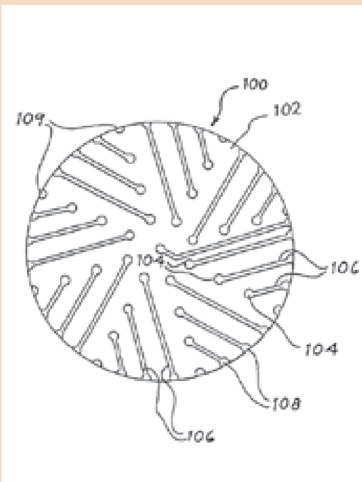
Mathematicians have checked the validity of both statements by computer for all numbers up to 19 digits, and they have never found an exception. Moreover, the larger the number, the more ways exist to split it into a sum of two other numbers—let alone three. So the odds of the statements being true become better for larger numbers. In fact, mathematicians have demonstrated that if any exceptions to the strong conjecture exist, they should become increasingly sparse as the number edges toward infinity. In the weak case, a classic theorem from the 1930s says that there are, at most, a finite number of exceptions to the conjecture. In other words, the weak Goldbach conjecture is true for "sufficiently large" numbers. Tao combined the computer-based results valid for small-enough numbers with the result that applies to large-enough numbers. By improving earlier calculations with "lots of little tweaks," he says, he showed that he could bring the two ranges of validity to overlap—as long as he could use five primes.

Next, Tao hopes to extend his approach and show that three primes suffice in all cases. But that is not likely to help with the strong conjecture. The weak conjecture is incomparably easier, Tao says, because by splitting a number into a sum of three, "there are many, many more chances for you to get lucky and have all the numbers be prime." Thus, a quarter of a millennium after Goldbach's death, no one even has a strategy for how to solve his big challenge. —*Davide Castelvecchi*

PATENT WATCH

Apparatus and methods for mapping retinal function: More than two million people older than 40 in the U.S. suffer from glaucoma. The disease—one of the leading causes of blindness—is the result of damage to ganglion cells in the retina. Early-stage glaucoma is treatable, and the earlier it is caught, the easier it is to reverse. But catching glaucoma is not easy, because it often starts at the edge of the retina, beyond our usual field of vision. The standard way of detecting it is decades old and involves placing a contact lens with a single electrode embedded within it on the eye. The subject is shown a series of light flashes, and the electrode picks up the electrical responses from the retina. "What's missing in that signal is any spatial differences in the health of the retina," says John Hetling, a researcher at the University of Illinois.

It is difficult for doctors to determine if one part of the retina is healthy and another part is not. Hetling and his team wanted to improve on the standard method. They are working on a lens that holds far more electrodes—between 33 and 57. These extra electrodes allow for diagnoses of a larger area of the retina in far less time. Their device, patent No. 8,118,752, could also help detect other retinal diseases caused by diabetes, hypertension, sickle-cell anemia and premature birth. —*Rose Eveleth*



COURTESY OF U.S. PATENT AND TRADEMARK OFFICE

SCIENTIST IN THE FIELD

"It's Almost Science Fiction"

Steven Chu on the futuristic batteries and "little weird" bacteria that will pave our way to energy independence

Is domestic energy independence a useful goal?
It's certainly a useful goal to strive toward energy independence. The good news is that three and a half years ago we were importing about 60 percent of our oil, and now it's around 45 percent. We see the trend going forward, decreasing even more. We are already largely energy-independent in terms of electricity generation, although some electricity comes from Canada.

We also see a flattening, perhaps even a decrease, in the use of transportation fuels as we go to more efficient automobiles. We see more diversification of transportation energy. Liquefied natural gas for long-haul trucks has already been shown to make sense. Private companies are investing hundreds of millions of dollars to build natural gas infrastructure. If you build it every 200 miles on the highway, you can capture a significant market, perhaps even half the market, and heavy trucks consume 20 percent of our transportation energy.

PROFILE

NAME
Steven Chu

TITLE
U.S. Secretary of Energy

LOCATION
Washington, D.C.

Does that mean we've given up on combating climate change?
No, absolutely not. This is all very consistent with climate change. Natural gas as a transition fuel is great. It's half the [carbon dioxide of burning coal]. We still need to figure out how to capture its carbon, which we need by midcentury no matter what the large source is [whether it is coal, oil or natural gas].

Renewable energy is getting cheaper and cheaper. Perhaps within this decade wind and solar will be as inexpensive as any form of new energy. Solar has already come down threefold in the past four years, and we believe it will come down twofold in the next decade.

In transportation, there will be a mix of electrification and next-generation biofuels and efficiency. If we get breakthroughs, it can be game-changing.

Where do you think such breakthroughs might come from?
Breakthroughs on the physics side will be in materials. The battery manufacturer Envia [Systems] announced a 400-watt-hour-per-kilogram battery. That's at least a factor of two more than the previous best. It still has to go through some more stages of testing. We are investing in other battery companies that will go another factor of two beyond that.

Biofuels are a little bit further out only because your competition is oil. Early-stage research sponsored by the Department of Energy has microbes you can feed simple sugars and out pops diesel fuel. Another company is using photosynthetic bacteria and swapping whole genomes and metabolic pathways. [The microbe] generates long alkane chains that are the immediate precursors to diesel fuel. It's 5 to 10 percent energy-efficient, whereas a typical plant is only 1 percent efficient. This is a little weird bacterium or yeast. In the past 15 years or so I've gotten into biology like this. I follow it with avid interest. It's really almost science fiction.

What have you learned about how the government should fund new energy companies?
In areas of rapidly moving technology, you have to be increasingly careful when assisting in deployment. Some things happened so rapidly that nobody anticipated them. For example, the price of photovoltaics dropped 80 percent in [recent years] and 40 percent in another year. Those prices have now stabilized.

It's very important that the U.S. remain a player in this technology [photovoltaics]. We invented a lot of this stuff [such as modern solar cells]—you name it. We still have the capability of outcompeting.

I knew full well coming in that unexpected things can happen. [Technology] leads can be lost. It's a very competitive world out there. For example, we invented the airplane, lost the lead, then came back.

We are still highly competitive in all areas of high-tech manufacturing, including most new energy. We need to choose our battles, but a lot of them we can—and should—win. *—David Biello*

STAT

8 *inches*

The approximate average global rise of sea levels since 1880.

13 inches: Amount by which sea levels could rise over the next 40 years, according to one estimate. An analysis published in March in the journal *Environmental Research Letters* shows that ocean levels are rising faster than ever before.

IMKE LASS *Redux Pictures*

COMMENT AT ScientificAmerican.com/may2012

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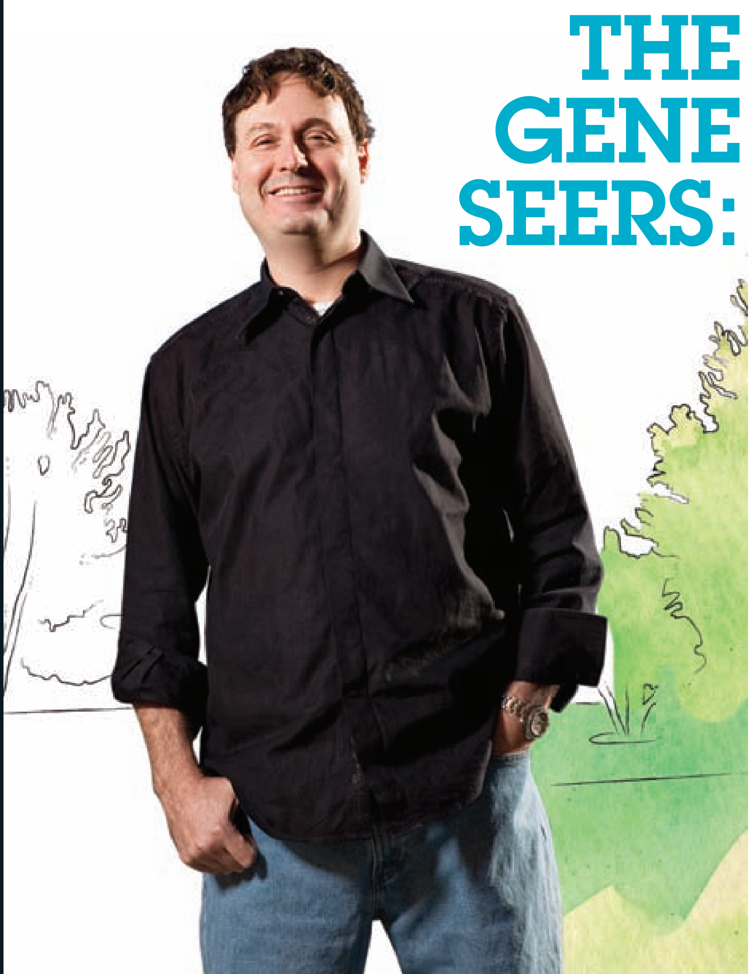


THE GENE SEERS:

Q&A WITH GREG LUCIER & JONATHAN ROTHBERG

Perhaps the most exciting frontier in medicine today is the emerging field of personal genomics: the use of detailed knowledge about a patient's individual genetics as a guide to better prevention and treatment. Much of what makes it possible are the rapid improvements in the sequencing technologies that determine the precise arrangement of paired nucleotide bases in someone's DNA that defines his or her genome. Between 1990 and 2003, the U.S. federal government spent roughly $3 billion to produce a final draft of the first human genome (and to amass a wealth of research findings vital to making sense of it).

This year, the price for sequencing a genome will fall to just $1,000 with Life Technologies' new Ion Proton technology. Medical policy planners have long considered the $1,000 price tag to be a crucial threshold because it puts the cost of sequencing a genome roughly on a par with that of an MRI scan—which greatly improves the chances that insurers might reimburse for it.

To get their perspectives on personal genomics, we spoke with Greg Lucier, the CEO and chairman of Life Technologies, and Jonathan Rothberg, the CEO of the company's sequencing division, Ion Torrent Systems. This conversation is edited from several interviews and discussions that took place in the days surrounding the Digital Health Summit at the 2012 Consumer Electronics Show (CES), where Life Technologies debuted its new Ion Proton sequencer.

THE CONVERSATIONALISTS:

- **Jonathan Rothberg is the CEO of the Ion Torrent division of Life Technologies**
- **Greg Lucier is the Chairman and CEO of Life Technologies**

Q: It's interesting that Life Technologies has chosen to make this momentous announcement about reaching the $1,000 genome here at the beginning of the CES, where people would traditionally expect to find out about new TVs, computers or appliances —not about cutting-edge biomedical technology. What's the significance of doing it here and now?

LUCIER: If you look back in history, most revolutions happened when a tool was created to make them happen. I think that's what this announcement about the $1,000 genome is today in terms of putting us on the path to genomic medicine. It allows this to happen in a very fast, economical way and will bring about a whole new level of information that doctors can use to make decisions with their patients.

The ability to read the molecules in our body as digital information certainly falls into this interesting, more general arena of monitoring the body digitally. Genomics just takes that to the nth degree, the next level. We're becoming more and more engaged in our own wellness, and electronics is enabling that. We saw many other applications here at CES today for physiological monitoring, EKGs, and things of that nature. So it's a very exciting vector for this CES, and I think you're going to see it grow quite demonstrably in the future.

In the past seven years we've learned more about the origins of disease at a genetic level than we did in the previous 30. But for genetics to really have an impact on health, we're going to have to enter into an era of collaborative medicine in which patients get sequenced and it becomes part of their electronic medical record. We'll be tracking patients and looking for correlations between their genes and their illnesses and how well they responded to treatments. Other patients and their doctors will be able to see anonymized forms of that data and benefit from what it helps to explain. So in this digital era, I'm very encouraged that collaborative medicine driven by genetic information will lead us even faster to ways to improve patients' outcomes.

ROTHBERG: First, I agree with Greg that this digital genetic information will be part of your medical record that also contains the digital information from your CAT scans, your MRIs, pathology reports, and so on. So partly we're here because your genome sequence is going to be part of your electronic medical record.

Second, in our sequencing technology, we leveraged the same CMOS technology that enables essentially all the devices that you see on the show floor. You have a chip in your cell phone that sees light, and it's what allows you to have a camera in there. We made a chip that saw chemistry instead of light! That was the key "aha!" moment.

We're leveraging that trillion dollar investment over the past 40 years in those chips, and the same supply chain, and of course, the same Moore's Law. That's why it was inevitable that we'd get the cost for sequencing a whole human genome in a couple of hours down to $1,000. And that's why we selected Gordon Moore himself [co-founder of Intel, for whom Moore's Law is named] to be the first person to be completely sequenced with the technology, which we published in *Nature* last year.

Q: So, as with Moore's Law in computing, should we expect to see the cost of sequencing continue to drop?

ROTHBERG: Absolutely. It's something I have to fight constantly, but people keep saying that DNA sequencing is going faster than Moore's Law. That's an illusion. With the switch to new, CMOS-based methods, we're just catching up to what 40 years of accumulated Moore's Law has done for progress in electronics. We estimate that we'll probably be fully caught up somewhere around 2014, and then the progress and cost of sequencing will progress along with all other costs that are driven by Moore's Law.

Q: As you know, one of the concerns often voiced is that sequencing technology may start pumping out genomic information faster than we know what to do with it. That we'll be wallowing in sequence data that we can't interpret intelligently, and that this will prove counterproductive to people's health or well being. You seem to be more optimistic.

ROTHBERG: I'm optimistic for two reasons. One, Life Technologies in particular is putting a huge amount of work into it. We have a new effort with Carnegie-Mellon University to develop better artificial intelligence agents, like Siri [on Apple's iPhone] or Watson [IBM's *Jeopardy!* game-playing computer], that would help a doctor to access and interpret genetic information with more expertise. The other reason is because the more sequencing we do of individuals and the more we correlate gene sequences with their medical records, the more we know. If I sequence one person, I don't know anything. But if I sequence 100,000 people with cancer—or with cardiovascular disease or with autism—and I have their medical records and I understand how they respond, I could know all about complex diseases.

Recently, I raised that same problem you did to a group of 16 computer scientists at Carnegie-Mellon who contributed three of the modules to Watson's memory, and they told me that I shouldn't worry about it. They felt reasonably confident there was enough progress going on in using unstructured data to apply it to genomic information and to mine for relevant answers in pathology reports, radiology reports, and so on. The tools could interact with physicians to help them along the way.

"One in five cancer drugs is effective today. That is just not an acceptable rate."

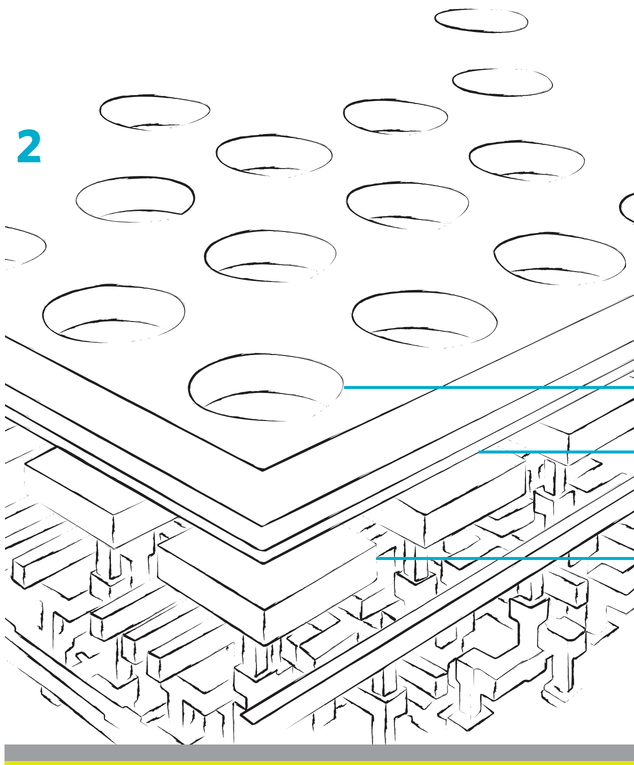
Q: You've mentioned that in applying our newfound genomic information to specific problems, cancer is low-hanging fruit. What makes cancer so well-suited to be a target?

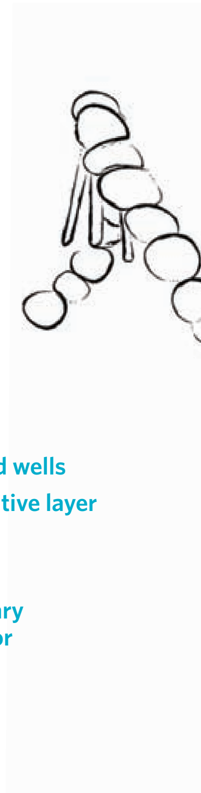
LUCIER: Cancer is a disease of the DNA. It is a bit ironic that we haven't been reading the DNA until now. But here we have a tool that will help us to see the very thing that's causing the disease, and in the future the physician can match up the specific defects in the DNA with the right therapeutic to help an individual patient with a particular malignancy.

One in five cancer drugs is effective today. That is just not an acceptable rate. And cancer progresses; time matters. Having an accurate ability to read the DNA and to select the right therapeutic in a timely fashion could make a world of difference.

You can't believe the groundswell of referrals I get, people calling me constantly: "I have a brother" or "I have a cousin, 1

2





1. The Life Technologies' chip-based technique sequences genomes in a massively parallel way.

2. The sequencing chip carries a high-density array of micromachined wells, each of which holds a single strand piece of template DNA. Beneath the wells are an ion-sensitive layer and a proprietary sensor layer (above).

3. A growing DNA strand complementary to the template selectively takes up nucleotides entering the well. That reaction releases a hydrogen ion (above right). The sensor detects this ion, signaling the new base in the sequence

can you please make the introduction to this doctor?" It shows you that people are getting activated. They are becoming aware. They don't want just to place their care in the hands of the doctors and wait for the doctors to reach an understanding that may or may not help them. That's what has to happen now, quite frankly. I think we're on this irreversible course. People are starting to understand genetics to a certain degree, and they will learn more. They will start talking to their doctors and they will expect their doctors to understand, too, and do something about their conditions.

Q: This kind of personalized genomic medicine isn't an abstract topic for either of you, is it?

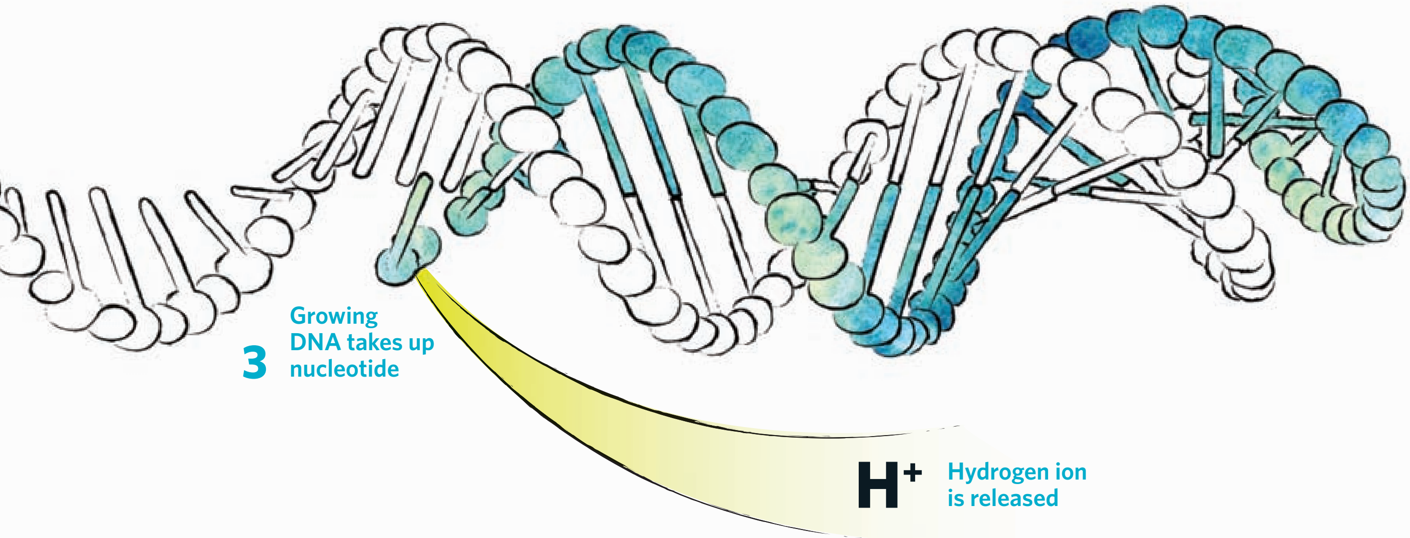
ROTHBERG: When my newborn son developed breathing problems and the doctors weren't sure whether it was something genetic, that was the moment when I understood what personal medicine meant. [See "The Inside Story of a Sequencing Chip," on the facing page.]

LUCIER: Two years ago, I had my own genome sequenced and spent time with some of Life Technologies' researchers going over the results. It turns out that I carry a mutation that raises my risk for an unusual type of Parkinson's disease. That's a good thing for me to know and watch out for as I get older.

What was also significant about that, though, is that my mother happens to have been suffering from a degenerative neurological condition that had been diagnosed as multiple systems atrophy. My results tipped us off to check her for the same mutation, which led us to discover that she has it too, and that her illness is really Parkinson's. That didn't point us to a cure for her, but it did suggest ways to improve her treatment.

My genome also showed that I carry the BRCA1 mutation that increases the risk of breast and ovarian cancer. We don't know yet whether my daughter has inherited it from me, but until we do, I'm going to urge her to get regular mammograms as a precaution when she gets older. •

** Ion Proton Sequencer is for research use only. Not intended for human diagnostics purposes*



THE INSIDE STORY OF A **SEQUENCING CHIP**

Inventors don't always recall exactly how or when they had the "eureka!" moments that led them to their breakthroughs. Yet Jonathan Rothberg, who created the system that will enable Life Technologies to sequence a whole human genome in hours, remembers precisely. He credits both of the inspirations to his son, Noah: "The first because he was sick and the other because he was cynical!" Rothberg says.

"Prior to his birth, I thought I was on top of the world," he says. Back then, he was the founder and CEO of the company then called CuraGen, which was mining the cumulative information pouring out of the world's genome projects to develop new drug candidate compounds. But in 1999, shortly after his birth, Noah turned blue because of breathing difficulties and was rushed to intensive care. Doctors were not sure whether his problem might be genetic. Helpless in the hospital's waiting room, Rothberg says, "I was not interested in the human genome as a map for humanity. I really only cared about my son's genome. That was really the moment when I understood what personal medicine meant."

Then Rothberg noticed a photograph of a Pentium microprocessor on the cover of a magazine in the waiting room. He suddenly made a mental connection to genome sequencing and realized, he says, "everybody had been doing it wrong." Big sequencing efforts had always involved scaling up the number of sequencing machines involved to increase output, like hiring more people to work in a factory. But Rothberg saw that semiconductor technology should make it possible to execute and monitor many chemical sequencing operations simultaneously on a chip. After Noah recovered—his problem turned out not to be genetic—Rothberg developed those ideas into the technology on which the company 454 Life Sciences was based.

The second pivotal moment was in 2007, when Rothberg says he was bragging to his son that he had just read the genome of the legendary biologist James Watson. Noah's unimpressed response was, "Sure would be more lucrative to read minds."

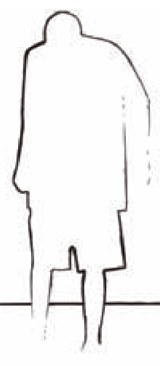
The comment made Rothberg realize that an inefficiency in his sequencing approach was that it relied on chemical processes that emitted light detectable to a chip to signal the sequencing results. "What we needed was a chip that could see chemistry instead of photons," Rothberg says. The semiconductor devices called ISFETs (ion-sensitive field effect transistors) invented in 1970 by Piet Bergveld offered a way to do it.

Rothberg's Ion Torrent Systems team created an ISFET-based sensor chip similar to the light-sensitive one in a smartphone's camera, except that the surface is an array of microscopic wells. (In the original chip, 400 wells were packed into an area like the cross-section of a human hair; in the new Proton chip, the same area holds up to 10,000 wells.) Each well acts like a tiny beaker with a pH meter in it. Single-strand bits of DNA from the genome to be sequenced sit in each well as a template, along with the enzymes and other requirements to grow a complementary matching strand of DNA. During the sequencing process, solutions containing one DNA base sequentially wash through the wells. If that base matches the next open position in the template strand, it attaches to the growing complementary strand. That chemical process releases a single hydrogen ion into the well. The ISFET at the bottom of each well specifically registers that change in pH, thus revealing the identity of one more base in that well's template DNA sequence.

> "What we needed was a chip that could see chemistry instead of photons."

DNA & THE DAWN OF DIGITAL MEDICINE

Three years ago, all the people whose DNA had ever been fully sequenced—all seven of them—could have fit in the waiting room of the average doctor's office. Today, the best estimates suggest the number of people with sequenced genomes is well in excess of 30,000. Three years from now, the total may be in the tens of millions. And most of those people will eventually end up in their doctors' offices, genomes at least figuratively in hand, asking about what the details of their DNA might mean for their current or future health.



Genomics, a field that has attained unparalleled prominence in biology research over the past few decades, is fast on its way now to becoming a routine part of medicine. Rapid advances in DNA sequencing technology are catalyzing that change. In early January, Life Technologies stole headlines with the announcement of its new Ion Proton Sequencer, a high-throughput device that is designed to read an entire human genome in two hours at a projected cost of $1,000—a goal that biotechnologists have been chasing ever since the completion of the first human genome sequence a decade ago.

"Before this point, the machines were too big, far too expensive, and took weeks if not months to get the results," remarks Greg Lucier, CEO and chairman of Life Technologies. "And now, literally, this machine is the size of a printer that could be on your desktop."

Yet the new simplicity of sequencing is only part of the story. Genomics is converging with computing, wireless communications, sensors, imaging and new medical information technologies to create a framework for "digital health" that could transform the practice of medicine.

"Each individual is unique: we have our own biology, our own physiology, our own environment. And the way medicine is practiced today couldn't be further from that," observed Eric J. Topol, the director of the Scripps Translational Science Institute, during his opening remarks at the Digital Health Summit at the 2012 Consumer Electronics Show in January. As a result, he says, "We spend over $300 billion a year on drugs in this country alone. Most of that, believe it or not, is wasted, because we don't match up the right drugs at the right dose with the right patient."

Topol argues in his new book, *The Creative Destruction of Medicine: How the Digital Revolution Will Create Better Health Care* (Basic Books, 2012), that genomics and the rest of the new digital health infrastructure will make it possible to understand any individual's health more profoundly and comprehensively than ever before. Consumers empowered by the new technologies and unprecedented access to their own medical information, he thinks, will transfigure healthcare, with colossal benefits in better outcomes, reduced suffering, and saved costs.

His vision is one that growing numbers of people, inside the genomics field and out, are coming to share. Jonathan Rothberg, the CEO of the Ion Torrent division of Life Technologies and the inventor of its high-throughput sequencing method, emphasizes that personal genomics is a tool that only becomes useful in the context of an individual's full medical history, including specialists' reports, imaging records and other data. "But here's where I will be bold," he says. "I think that this new addition will be as important to human health as clean water, antibiotics and imaging."

TARGETED GENOME VS. WHOLE GENOME SEQUENCING

Genetic tests for diseases have been around for a long time, so one might wonder why it's a big deal that the technology has advanced enough to sequence all of someone's DNA inexpensively in a couple of hours. After all, of the three billion base pairs in DNA, only about 1.5 percent code for proteins, which is what most genetic defects seem to affect—so sequencing it all might seem like overkill. In fact, for several reasons, it is hugely important.

Most of what one might consider medical genetic tests, however, do not really look directly at the genes at all. Instead, they check body chemistry for the presence of proteins or other metabolites that signal whether certain genes are active. For example, the phenylketonuria (PKU) test performed on newborns looks for a compound in their blood that signals whether they can make the enzyme that digests the amino acid phenylalanine. The results of such tests show whether a gene is working but don't say much about what's gone wrong if it isn't. Genetic sequencing is potentially more accurate and can reveal precisely what mutation has shut down a gene—information that might be useful in devising a treatment.

Advances that make whole genome sequencing faster and affordable do the same for more targeted sequencing, too. Sequencing a panel of suspicious genes can become so easy that physicians stop needing to send DNA samples to expensive labs: they can do it themselves in the office with desktop equipment, maybe even while patients wait. The cost and ease of targeted sequencing can therefore potentially plummet.

For example, Life Technologies currently markets a product based on its $99-chip technology that looks at a targeted panel of 46 genes involved in tumor growth. In development, the company says, are ones that would look at a more comprehensive set of 400 cancer genes and at about 100 inherited diseases. (These products are currently only for research purposes, not medical diagnostics.)

"I think that this new addition will be as important to human health as clean water, antibiotics and imaging," Rothberg says.

Useful as targeted genetic tests can be, when used for diagnostics, they are a bit like searching at night for your keys under a lamppost only because the light is better there. The tests can confirm a physician's suspicions about what is wrong but they don't flag unexpected sources of trouble, such as any other mutations that might be disturbing a patient's physiology more subtly.

Whole genome sequencing, however, illuminates every corner of a patient's physiology and can suggest new hypotheses if the obvious causes for a medical condition don't apply. It also provides a single unified terminology for describing a patient—a lingua franca of base pairs, if you will—that all medical specialties can use to share detailed information.

As whole genome sequencing gets less expensive, it may eventually become a standard, preferable alternative to targeted sequencing or metabolic screening. People sequenced at birth (or maybe even prenatally) could have all their genetic information tucked into their medical records for reference throughout their lives. The interpretation of the genome record could constantly evolve along with medical science. Patients and their doctors could use it to tailor prevention measures that would head off potential medical problems.

And it is here that the genomic medicine movement merges with Topol's ideas of a broader digital health revolution now brewing—a revolution that intends to liberate all our medical information from the Bastille and arm us with devices that can make healthful use of it every day.

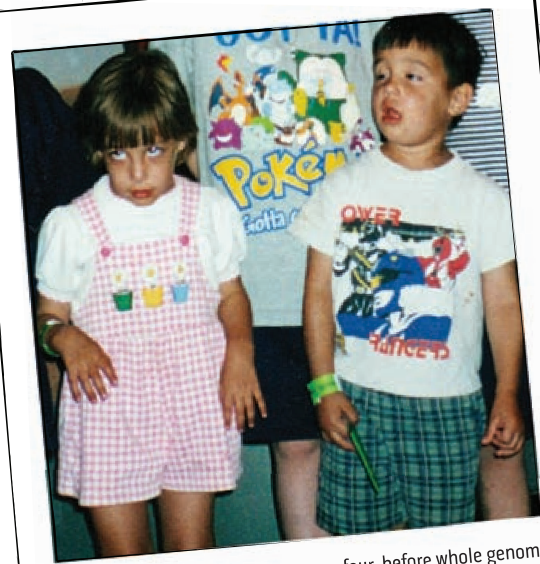
DRIVERS OF DIGITAL HEALTH

Several trends in concert are driving the rise of personal genomics and digital health. One is of course the increasingly molecular focus of modern medicine, in which being able to characterize a patient's state of health in terms of genetic information serves as a key to its management.

Digital health is also a fruit of Moore's Law, which relentlessly makes computing, communications and all other chip-related technologies faster, cheaper and more compact. Computing has always been instrumental in genome sequencing efforts but the development of chip-based sequencing techniques has enabled personal genomics to suddenly "leverage 40 years worth of Moore's Law," in Rothberg's words—and puts it in a position to ride the curve upward hereafter.

The advent of mobile digital technologies over the past two decades is playing a big part, too. Mobile technology offers largely unprecedented opportunities for collecting and distributing information on the go, so measurements of people's health under all conditions can be more complete and continuous than when medical instruments were anchored in one location.

Another factor might be the modern tendency to look for health answers outside the traditional medical establishment. For better or worse—or rather, for better *and* worse—unsatisfied consumers are questioning their physicians' authority and looking for help within circles of their peers with relevant knowledge and experience. "Patients with rare conditions often understand more about their conditions than their physicians do," says Jesse Dylan, the founder of Lybba, a non-profit that advocates for open source healthcare. Social media and the Web are instrumental in establishing those peer-to-peer connections easily.



Above: Alexis and Noah Beery at age four, before whole genome scanning diagnosed their condition accurately. At right: The twins at age 14.

THE CASE OF THE BEERY TWINS

If the cause of whole genome sequencing and personalized medicine needed poster children, they might be the 15-year-old fraternal twins Alexis and Noah, offspring of Retta and Joseph Beery of Encinitas, Calif. Joe, who is the chief information officer of Life Technologies, joined the company in 2008 partly because the twins' difficult medical history made him appreciate how much diagnostics needed to improve.

> "It was all connected," Retta says. "And the only way we found that out was through whole genome sequencing."

At age two, Alexis and Noah, who had been constantly nauseated and colicky from birth, were diagnosed from an MRI as having cerebral palsy. But Alexis's condition started to get worse, and she showed symptoms inconsistent with that diagnosis. "At age five and a half, our daughter started losing the ability to walk during the day," Retta recalls.

Retta, who was studying everything she could find that might contain a clue about what was plaguing her children, eventually read a magazine article that mentioned a rare nervous disorder called a dystonia that mimicked cerebral palsy and which could be treated with the Parkinson's disease medication L-dopa. Doses of that neurotransmitter immediately allowed both children to function at a high level, she says.

Then in 2009, a chronic cough that had bothered Alexis for years suddenly blossomed into a severe breathing problem. "We almost lost her on many occasions over a period of about 18 months. We had paramedics in our house. We had taken her to the ER. Every other week we were going through this," Retta says. "We never knew if she was going to make it through the night." No one could figure out why Alexis couldn't breathe, Retta adds, but her neurologists were convinced the respiratory problem was unconnected to her motor problems.

Desperate, the Beerys reached out through Life Technologies to scientists at the Baylor College of Medicine as part of a research study to do whole genome sequencing on Alexis and Noah to see if it could find the root of their problems. The Baylor group agreed, and eventually identified a single mutation responsible for both sets of symptoms: one that lowered not only the children's L-dopa levels but also those of a second neurotransmitter, serotonin.

Doctors put Alexis on a new medication that restored her levels of both chemicals. Her breathing returned to normal and within weeks she was back to participating in school track and field events. (A smaller dose of the same drug also helped Noah.) "It was all connected," Retta says. "And the only way we found that out was through whole genome sequencing."

FIRST TARGET: CANCER

Rare inherited disorders are obvious targets for personalized genomic medicine to go after because of the good that it could do, as the Beery twins' story attests. The condition that many of the medical genomics innovators are making a prime focus of their work, however, is far more common: cancer.

Cancer, after all, is fundamentally a problem of genes gone wrong, of cells acquiring mutations that make them divide uncontrollably and careen harmfully through the body. According to a report by the President's Cancer Panel of the National Cancer Institute in 2010, 41 percent of Americans will develop cancer at some point in their lives and about 21 percent will die of it. Progress against the disease—which biomedical researchers increasingly view as a highly diverse set of conditions rather than a monolithic entity—has been frustratingly mixed and on the whole disappointing, despite decades of detailed biological study.

Much of the biomedical establishment believes the problem with treatment is that the effectiveness of chemotherapies varies considerably with the genetic make-ups of individual patients' tumors. Given that a course of chemotherapy can easily cost tens of thousands if not hundreds of thousands of dollars, even the financial burden to society of prescribing inappropriate drugs is heavy—let alone the cost in needless suffering.

So developing targeted therapies against cancer has become a high priority. A shining and oft-cited proof of the concept is Novartis's drug Gleevec (imatinib) for chronic myeloid leukemia, which very specifically attacks one enzyme found in those malignancies but not in most dividing cells. When used by patients whose leukemia is caught early on, the drug is nearly 100 percent effective. A number of other targeted therapies, such as getfitinib for certain lung cancers and trastuzumab for some breast cancers, have also been developed.

What holds true for Gleevec may apply to most cancer drugs. Last summer at the annual meeting of the American Society of Clinical Oncology, Apostolia-Maria Tsimberidou of the University of Texas M.D. Anderson Cancer Center presented the results of the largest study to date on matching specific drug therapies to mutations in patients' tumor cells. She and her colleagues reported that in patients with unmatched treatments for inoperable or metastatic cancers, the response rate was only about 5 percent and median survival time was nine months. In patients with matched therapies, the response rate soared to 27 percent and they survived on average 13.4 months, about 50 percent longer.

It's widely suspected that better genetic guidance would similarly benefit cancer prevention by identifying people who are most at risk for particular malignancies. Mobile devices might then offer timely reminders or other forms of support that would help individuals keep on the healthy regimens prescribed for them.

TURNING DATA INTO USEFUL ADVICE

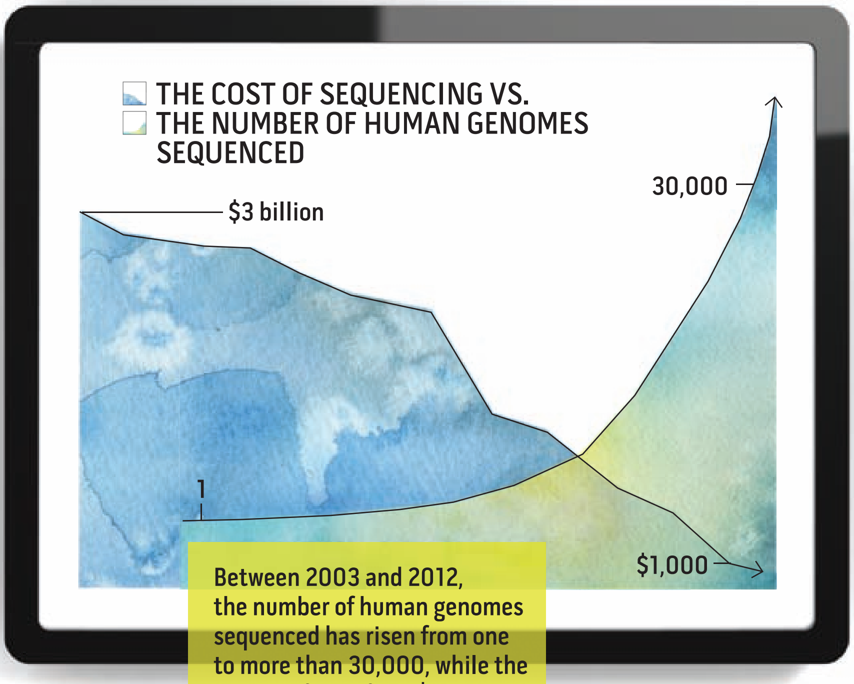
The digital movement is poised to process unprecedented amounts of health data about unprecedented numbers of people. But gathering and moving data around isn't the goal—achieving better health outcomes is.

Anand Iyer, president and COO of the digital health solutions company WellDoc, points out that many of the monitoring capabilities and potential interventions that could improve people's health already exist. "The raw materials are there," he says. "The problem is, the raw materials aren't available where the patients are, when and how they need it." The key challenge for companies in the digital health space, he says, is to use people's personal information—not just their medical data but seemingly unrelated facts like their social media preferences—to create and deliver "bite-size chunks" of "actionable knowledge" at exactly the right moment. "We need to take what we have and we need to deliver it in new ways," he says.

Christine Robbins, president and CEO of Body Media, agrees. "What action do I take to help change behavior? Because that's what we're all trying to do," she says. Individual users might want behavioral changes that would help them get fit; meanwhile, insurance companies want the population to adopt behaviors that would bring down healthcare premiums.

Smart design will also play a crucial role in making sure digital health offerings are actionable, says Robert McCray, CEO of the Wireless HealthScience Alliance. Everything, from monitoring devices to messaging systems, will need to be inexpensive and simple to install and use. "No IT degree required," he jokes.

That kind of simplification or demystification will be especially important in systems that patients—and their physicians—will need to make sense of the huge, sprawling complexities



Between 2003 and 2012, the number of human genomes sequenced has risen from one to more than 30,000, while the cost has fallen from $3 billion to only $1,000 associated with genomic data and all the biomedical records associated with it. "Human factors is the biggest issue that we have, and where there is a big opportunity," McCray says. Good design can inform people without overwhelming them. By analogy, he cites the engine temperature indicator on a BMW automobile, which is just a simple red light that doesn't say what the temperature is. "As long as you trust that red light, or the amber one that tells you you're getting closer to needing an oil service, that's all you need," he says. "As a consumer, you just need to trust the application and the source."

When people act on the basis of highly personalized data, they may not be doing it alone. People with shared health problems are banding together more often in online communities such as PatientsLikeMe and CureTogether to educate themselves and learn how to manage their conditions: digital technology makes it ever easier to find fellow sufferers and to share information.

The digital movement is poised to process unprecedented amounts of health data about unprecedented numbers of people.

"We've seen a wave of people wanting to take action," says Robbins, who pins her company's recent success on its decision to offer consumer solutions, not just medical or research products. The social component of being able to share one's medical data, she says, brings "a whole new level of accountability" and engagement that can help keep people on track with the health plans they choose.

The rise of personal genomics will be highly significant in this evolving conversation, says Jesse Dylan. "What it's going to make possible is for groups of patients to gather together and actually start to understand the underlying reasons [for their illness] in their DNA."

DECIPHERING GENOMES

Consumers aren't the only ones who need to trust and understand the information emerging from genomic studies, however. The scientists need to understand it first, and the challenge of interpreting genome data—of making meaningful associations between specific DNA sequences and particular health conditions, amidst all the other genetic and environmental influences potentially confounding them—has always been technically and financially daunting. Even if the cost of sequencing a person's genome has fallen to $1,000, making medical sense of it still involves an analysis that can cost hundreds of thousands of dollars.

Rothberg, for his part, thinks the interpretation problem will prove manageable. First, he dismisses the objection "that the sky is falling" because the sheer volume of required data storage will overwhelm data centers. He points out that, in keeping with past methods, genome sequences have often been stored as full photographic images of electrophoretic gels, much as astronomers have saved compilations of images of the sky. Geneticists, however, should not have to "find the sequence in the images," he argues: switching to digital sequencing techniques and saving the results as just an outputted string of bases would hugely reduce the amount of storage needed.

He adds that it shouldn't be necessary to store a complete genome for everyone. Any one person's sequence will differ from the canonical, reference version of the human genome at only about 24,000 sites, and it will probably hold only about 400 differences that seem unique. "That's not information overload," he says.

Progress on computerized tools that can comb through databases of genome information and make the important correlations is also coming, he believes, thanks to big attacks on the problem at Carnegie-Mellon University and other institutions. Furthermore, Rothberg argues that genomic science will benefit from synergies as the archive of sequenced genomes grows: the ability to check genes across an entire population and to match them with people's medical histories will make it easier to discover the genetic roots of specific conditions.

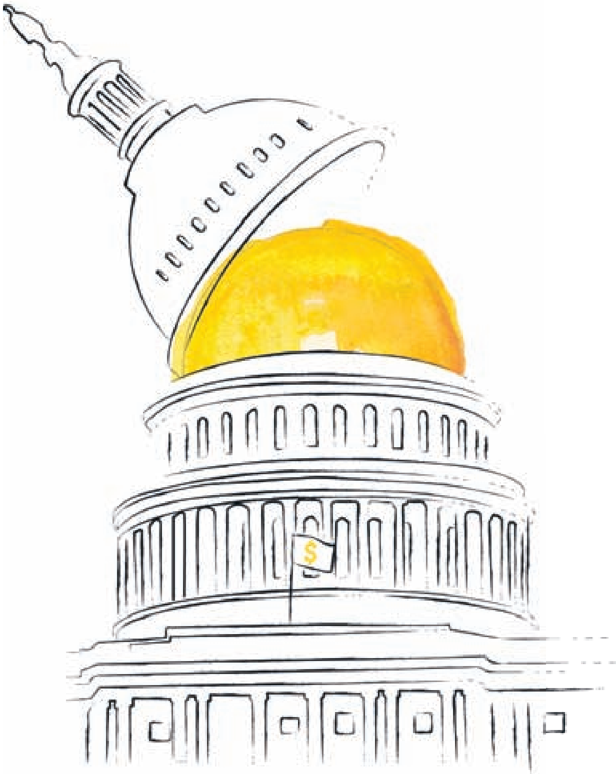
The catch, of course, is that much more still needs to be done to make medical records open and searchable, not just within and between institutions but also between different medical specialties. Jesse Dylan of Lybba thinks that future research may want to extend beyond defined medical records—not just to genome sequences, MRI scans and vaccination records, but to Facebook status updates and Instagram photos as well. "We're collecting all sorts of data in all kinds of ways that have never been imagined before," Dylan says. "And if they can't talk to one another, we won't get the best medicine that we possibly could."

PAYING FOR PROGRESS

If any thorny issue might derail the movement toward digital health, it might be the prospect of the expense. One way or the other, new digital health devices and services need to be paid for, either by insurers or by consumers directly. "We all want quality healthcare. But at the end of the day, we have to be able to afford it all," says Reed V. Tuckson, executive vice president and chief of medical affairs for the UnitedHealth Group. "And the cost escalation issues are very daunting and very challenging."

He notes that the highly regulated healthcare markets haven't always reflected individual consumer demand. He expects considerable pressure to continue to be put on the gatekeepers of health-related spending to make sure that their decisions reflect good comparative value.

But Tuckson is encouraged that cost doesn't have to put a chokehold on digital health innovation because society can meet the challenge in more than one way. Payers could be cautious about making sure that new technologies truly have worthwhile benefits and don't just inflate costs, he says, but also "because the cost challenges are so great, it provides a fertile medium for innovations to reduce those costs."



Many entrepreneurs in digital health are confident that, whatever the upfront costs might be, their products will end up sharply reducing medical costs by improving prevention and better matching drugs or other therapies to the specific ills of individual patients. Genomic information is clearly supposed to play a crucial role in achieving that goal.

"Employers today in the U.S. can't afford double-digit health care cost increases any longer," Lucier says. For that reason, he believes that aside from everyone's desire for better treatment outcomes, natural financial incentives flow from the potential of genomic information to cut billions of dollars out of healthcare costs by better tailoring drug treatments to patients. "Innovation actually leads to lower healthcare costs," he says.

"We spend so much money today on people getting therapies for which they are not appropriate. But more importantly, people are not getting the care that they need and are being subjected to side effects that they should not have to experience," Tuckson says. The goal should be to "identify that patient who is at risk really early and then use new digital, behavioral, supportive technologies to send a message that, 'You really are at high risk. This is not determined because of a population model or population-based assumptions. This is *your* genomics. And we can tell you what *your* risks are.'"

INVESTING IN THE REVOLUTION

Keeping healthcare affordable is only one of the complex economic variables that will determine whether the dream of genomically informed, personalized medicine materializes. Another is that neither the science nor the technology of personal genomics is yet so settled that most businesses can easily start offering services in the area. Much as U.S. federal investment into molecular biology research during the 1960s and '70s paved the way for the later biotech boom, further robust government investment—by the U.S. and other nations—into genomics, bioinformatics, and related areas will be crucial for speeding personalized medicine into reality.

As Margaret A. Hamburg and Francis S. Collins noted in their 2010 article "The Path to Personalized Medicine" in *The New England Journal of Medicine*: "When the federal government created the national highway system, it did not tell people where to drive—it built the roads and set the standards for safety. Those investments supported a revolution in transportation, commerce, and personal mobility. We are now building a national highway system for personalized medicine, with substantial investments in infrastructure and standards."

Therapeutics emerging from personalized medicine also may face severe obstacles. In theory, personal genomics could someday make it possible to prescribe a course of treatment perfectly optimized for a single patient. But as the target population for a treatment shrinks, finding appropriate ways to test its safety and efficacy gets harder and more expensive, too. Therapies that might be extremely effective for relatively few patients might risk getting caught in a regulatory limbo impeding their use outside of research settings. Insurers, too, might balk at seemingly thin evidence that a personalized treatment is worthwhile.

Further robust government investment... will be crucial for speeding personalized medicine into reality.

Meanwhile, the pharmaceutical industry has largely been built on a model of developing drugs that work well for large patient populations. If it costs roughly a billion dollars to bring a new drug to market, companies may deem it impractical to turn certain genomic discoveries into drugs. It's entirely possible, of course, that genomics research may help to lower those development costs, in part by identifying subgroups of patients who would strongly benefit from drug compounds that failed for the general population. Nevertheless, personal genomics could conceivably suggest a vast new number of "orphan drugs" that no one is prepared to develop for the sake of too few patients. Government support might therefore become important in helping to bring some of these potential treatments to fruition.

Notwithstanding these hurdles, however, the confluence of social, economic and technological factors favoring the emergence of personal genomics as an important part of how people will manage their health—with and without the direct involvement of traditional medical gatekeepers—seems all but irresistible. As Topol summarized the situation in *The Creative Destruction of Medicine*, "The foundation for genomic medicine has been laid. The revolution is ongoing: even though it has taken longer than initially projected, we are moving irrevocably forward in the second postsequence decade. Routine molecular biologic digitization of humankind is just around the corner." •

TECHNOLOGY

Does Digital Piracy Really Hurt Movies?

Two economists untangle the relation between illegal downloads and ticket sales

The shadowy nature of illegal media downloading makes it difficult for researchers to analyze the true relation between piracy and lost sales. Does every movie download represent a theater ticket left unpurchased, as the movie industry contends? Or are most downloaders people who never would have bought a ticket in the first place?

Two researchers have come up with a clever strategy to untangle one cause-and-effect relation. Economists Brett Danaher of Wellesley College and Joel Waldfogel of the University of Minnesota noticed that Hollywood studios often wait weeks after the U.S. premier before releasing a movie overseas. During that time, movie fans in foreign locales can find the film on BitTorrent-based file-sharing sites but not in their local theaters. If online piracy displaces ticket sales, these release lags should hurt a movie's international box-office receipts.

The researchers compiled a database of the weekend box-office returns for the top 10 movies in 17 different countries over three years. They then split the data into two groups: movies released before BitTorrent became popular and those released after. Controlling for everything else that might affect the returns for a movie, the researchers found that post-BitTorrent films made less money than pre-BitTorrent films. The longer the lag, the more they lost.

More damning, the genres most popular with online pirates suffered the most. "After BitTorrent, the effect of release lag on science-fiction and action movies is much greater than it is for other genres," Danaher says. He estimates that this type of piracy led to a $240-million annual drop in weekend box-office receipts in the 17 countries studied.

Of course, the study also proves a contention of piracy apologists: people turn to online piracy when that is the only way they can view the content. Danaher mentioned another episode from 2007, when NBC, in a contract dispute with Apple, suddenly pulled its content from the iTunes store. Traffic in pirated NBC content exploded. New laws may help steer people away from illegal downloads, but content providers need somewhere to steer them to. —*Michael Moyer*

COURTESY OF SATHYABHAMA DAS BIJU *University of Delhi*

WHAT IS IT?

This curled-up critter is one of seven new species of limbless amphibians found recently in the soil of northeastern India. It took researchers more than 1,000 hours of digging to discover all seven in 58 locations throughout the region.

This is not the first species this team has discovered. Sathyabhama Das Biju of the University of Delhi and his group have described 48 species. Biju worries, however, that many of his new species are in danger from the constant spread of development in northern India. —*Rose Eveleth*

Illustration by Thomas Fuchs

SPACE

Not Ready for Takeoff

A recent report from Russia's space agency sheds light on a string of recent failures

GROUNDED: Phobos on the launchpad.

Last November, Russia launched a widely anticipated mission to the Martian moon Phobos. The craft would gather samples from the moon's surface to help determine if future space crews could obtain valuable supplies of oxygen there en route to Mars. For Russia, the mission was supposed to mark a "cavalry charge" that would redeem a quarter-century of interplanetary impotence. Instead it turned into a cosmic humiliation when the craft died shortly after takeoff and fell back to Earth.

Phobos was part of a series of recent disappointments for Roscosmos, the Russian space agency. Last August a Progress supply ship headed for the International Space Station crashed. Just a week before, an expensive, new-model communications satellite was lost because of a guidance coding error, and early in 2011 another military satellite was sent into an improper orbit, possibly for a similar reason. The overall track record of Russian space launches is still not significantly different from that of other spacefaring nations, and the country did successfully ferry two groups of astronauts to and from the International Space Station late last year. But it is the nature of the apparent causes of the accidents—often amazingly inept human errors—that seems most alarming. A recent Phobos accident report has confirmed some Western analysts' worst fears.

The report, posted in Russian on the agency's Web site, obliquely admitted that two fundamental design flaws were at fault. First, most of the more than 90,000 overwhelmingly foreign-built microchips were never screened for radiation hardness and were purchased with full knowledge that they were not "space qualified." This supposedly allowed cosmic rays to knock out microchips inside the craft at exactly the wrong moment, which led the probe's computer to default to safe mode and await remedial commands from Earth that never came because of yet another design flaw. (Most Western experts believe, however, that the mission failed as a result of software flaws.)

Russian space officials have admitted to problems in the past. Valery Ryumin, a former cosmonaut and now deputy chief designer of the firm that builds and operates Russia's human space vehicles, told Echo of Moscow the day after the Progress crash that "of course, quality is worsening—we have to admit this." He added that "checks have become far less thorough than back in old Soviet days." The main reason for this trend is the loss of experienced workers and the industry's inability to attract qualified replacements in sufficient numbers.

In hopes of preventing further accidents of this type, Russian space officials seem to be falling back on Soviet-era practices, calling for more controls, more committees, more discipline and, where justified, more punishments. Whether this will attract and motivate desperately needed recruits is questionable. And they won't cure the problem at a time when Russian participation in American and European space missions is only set to increase.

—*James E. Oberg*

Oberg is an aerospace analyst and former engineer for NASA.

NUTRITION

Real Males Eat Yogurt

Probiotics may endow rodents with a "mouse swagger"

Last summer a team of researchers from the Massachusetts Institute of Technology set out to better understand the effects of yogurt on obesity. They were following up on the results of a long-term study from the Harvard School of Public Health that had suggested yogurt, more than any other food, helped to prevent age-related weight gain. The M.I.T. team, led by cancer biologist Susan Erdman and evolutionary geneticist Eric Alm, wanted to replicate the work in mice. The researchers took a group of 40 males and 40 females and either fed the animals a high-fat, low-fiber, low-nutrient diet meant to mimic junk food or fed them standard mouse meals. They then supplemented half of each diet group with vanilla-flavored yogurt.

Their goal was to understand how a probiotic diet affects rates of obesity and its related complications, including cancer. But "the most entertaining aspects of all this were things we didn't anticipate," Erdman says.

First, the scientists noticed that the yogurt-eating mice were incredibly shiny. Using both traditional histology techniques and cosmetic rating scales, the researchers showed that these animals had 10 times the active follicle density of other mice, resulting in luxuriantly silky fur.

Then the researchers spotted something particular about the males: they projected their testes outward, which endowed them with a certain "mouse swagger," Erdman says. On measuring the males, they found that the testicles of the yogurt consumers were about 5 percent heavier than those of mice fed typical diets alone and around 15 percent heavier than those of junk-eating males.

More important, that masculinity pays off. In mating experiments, yogurt-eating males inseminated their partners faster and produced more offspring than control mice. Conversely, females that ate the yogurt diets gave birth to larger litters and weaned those pups with greater success. Reflecting on their unpublished results, Erdman and Alm think that the probiotic microbes in the yogurt help to make the animals leaner and healthier, which indirectly improves sexual machismo.

The findings could have implications for human fertility. In ongoing work, a team led by Harvard nutritional epidemiologist Jorge Chavarro has looked at the association between yogurt intake and semen quality in men. "So far our preliminary findings are consistent with what they see in the mice," Chavarro says. —*Elie Dolgin*

GETTY IMAGES

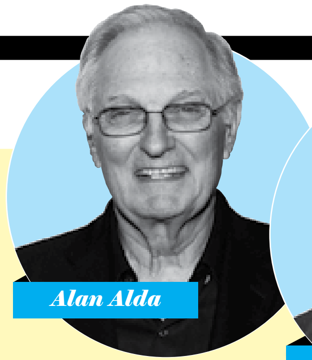
COMMENT AT ScientificAmerican.com/may2012

Best of the Blogs

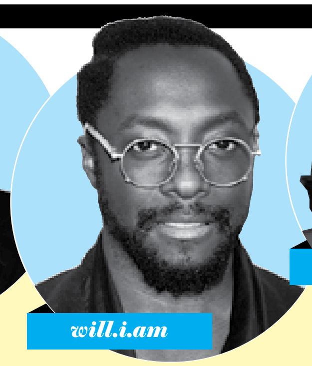
COMMUNICATION

Stars to the Rescue

Science as a new cause célèbre



Alan Alda



will.i.am

Björk

In magazine reporting (and maybe science blogging), they say three events suffice to indicate a trend. So let me announce a new trend: popular entertainers are sticking up for science. Here are three trend-setting entertainers turned notable science advocates.

Actor Alan Alda wrote an editorial in *Science* this past March launching a science communication contest to be judged by 11-year-olds. He challenged scientists to write an explanation of what a flame is "that an 11-year-old would find intelligible, maybe even fun." Alda is also a founding board member of the Center for Communicating Science at Stony Brook University, which is hosting the contest.

Icelandic pop singer Björk gave a series of shows at the New York Hall of Science this February in support of her latest album, called *Biophilia*. She also helped to develop a series of classes for middle school students on scientific concepts mentioned in the album, like crystalline structures, lunar phases and viruses.

Earlier this year rapper will.i.am teamed up with Time Warner Cable to launch a competition called Wouldn't It Be Cool If ... (www.wouldntitbecoolif.com), encouraging 10- to 15-year-olds to submit ideas for inventions powered by math or science that would make the world "more awesome." Last summer will.i.am co-produced a back-to-school TV special called *i.am* FIRST—*Science Is Rock and Roll,* which promotes education, science and technology. In the process, he successfully goaded singer Rihanna into tweeting "science is dope" to her millions of followers.

Of course, the bulk of our task to restore science to its rightful place in American society remains ahead of us. But I wonder if the good work done by these stars signals the beginning of a deep change in our culture. Is science starting to become cool again?

On the one hand, the outlook for science appears bleak. In February, Nina Fedoroff, now chair of the American Association for the Advancement of Science (AAAS), said at the 2012 AAAS Annual Meeting in Vancouver that she was "scared to death" by the antiscience movement. "We are sliding back into a dark era," she observed. "And there seems little we can do about it. I am profoundly depressed."

I've started to think that the recent celebrity interest in science is partly our own doing. Maybe celebrities tend to sympathize with struggling groups that show a kind of helplessness, like endangered animals and abandoned children. And maybe scientists have been seeking that kind of sympathy, consciously or unconsciously.

Federoff joins a chorus of scientific voices begging for aid. A report from the Union of Concerned Scientists came out this February called *Heads They Win, Tails We Lose: How Corporations Corrupt Science at the Public's Expense.* And you've probably heard of the 2010 report published by the National Academies Press called *Rising above the Gathering Storm, Revisited: Rapidly Approaching Category 5.*

Branding scientists as a kind of endangered species—that's probably not a marketing strategy I would have suggested we employ. But at the moment, in Hollywood, it seems to be working.

—Marc Kuchner

Adapted from the Guest Blog at blogs.ScientificAmerican.com/guest-blog

TECHNOLOGY

How to Tell Who's Tracking You Online

A new tool reveals your virtual footsteps and who's taking note

Mozilla has introduced Collusion, an add-on for the Firefox browser that shows you how companies are tracking you as you surf the Web. A cool visual demonstration of the software illustrates all the links that form as you crisscross just a few popular sites online, including IMDb, the *New York Times* and the Huffington Post. The software shows the connections among sites you visit and third-party tracking and advertising networks such as DoubleClick and Scorecard Research. It makes plain the invisible web that has been woven through the Web.

The software was created as a prototype by Atul Varma, who explained in a blog post that he "didn't know a lot about tracking myself, so I whipped up a Firefox add-on called Collusion to help me visualize it better. The results were a little unsettling."

Collusion will help you understand how you are being tracked online, but it won't stop it from happening. For that, you can disable third-party cookies on your browser and install other add-ons such as TrackerBlock. A number of Internet giants have also announced support for a "do not track" button, although that option may not become available until the end of the year.

—Michael Moyer

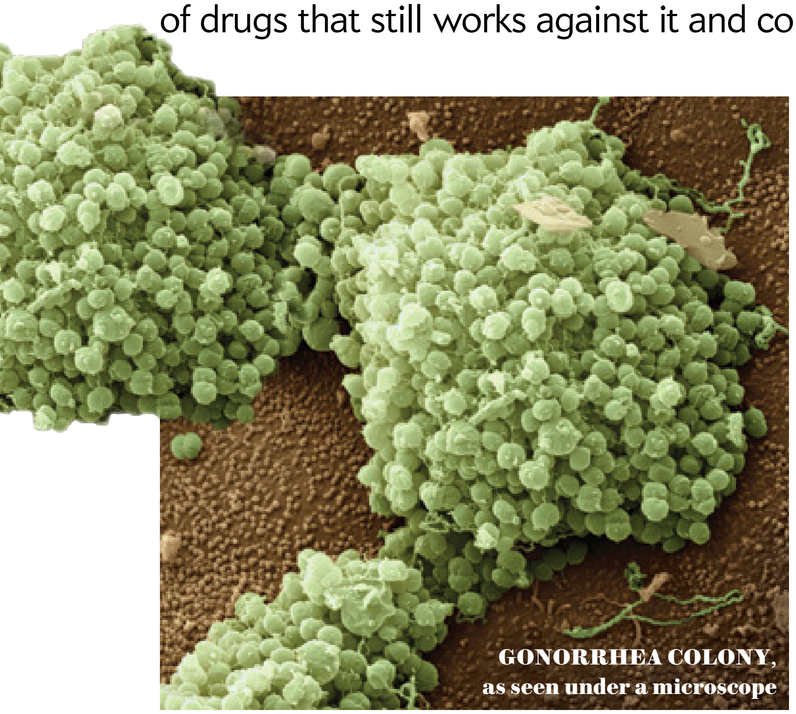
From the Observations staff blog at blogs.ScientificAmerican.com/observations

LEFT TO RIGHT: CINDY ORD *Getty Images*; GREGG DEGUIRE *Getty Images*; JO HALE *Getty Images*

Maryn McKenna is a journalist, blogger and author of two books about public health. She writes about infectious diseases, global health and food policy.

Return of the Clap

Gonorrhea, once a minor illness, is developing resistance to the last category of drugs that still works against it and could become untreatable



GONORRHEA COLONY, as seen under a microscope

JUERGEN BERGER *Photo Researchers, Inc.*

Mark Pandori was worried. It was 2008, and he had just read the latest in a string of reports from Japan. The articles all described patients infected with a particular strain of gonorrhea that was less susceptible than usual to an important class of antibiotics. Pandori, director of the laboratory at the San Francisco Department of Public Health, knew that gonorrhea had become resistant to other antibiotics in past decades. Each time, the resistance seemed to arise in Asia and spread to California. He wondered if something new was heading across the Pacific.

The latest report from Japan described a test that could identify resistant strains of bacteria by isolating and amplifying the culprit gene. Pandori tried the procedure on 54 samples of gonorrhea bacteria collected that year from men in San Francisco. Five samples, or 9 percent, contained the altered gene. When he analyzed the bacteria in the lab, he found that they—like the Japanese strains—possessed partial resistance to cephalosporins, the only antibiotics that still work reliably and inexpensively against gonorrhea.

Pandori and his research partner at the time, a health department epidemiologist named Pennan Barry, were alarmed and baffled. No physicians in the state had reported any difficulties treating patients with gonorrhea. Cephalosporin resistance had apparently infiltrated California without anyone noticing. Perhaps it had started spreading across the country as well.

Last summer a surveillance network run by the Centers for Disease Control and Prevention confirmed their fears. Using a different test, the CDC demonstrated that up to 1.4 percent of 5,900 gonorrhea bacterial samples from around the U.S. had diminished susceptibility to cephalosporins, meaning they would succumb only to unusually high doses. A *New England Journal of Medicine* editorial published in February said the occurrence of that partial resistance increased 17 times between 2006 and 2011. "The threat of untreatable gonorrhea is emerging rapidly," the editorial warned.

That threat is troubling for two reasons. First, gonorrhea is abundant: it is the second-most reported infectious disease in the U.S., with more than 600,000 new cases a year. Second, if untreated, it can cause widespread organ damage, pelvic inflammatory disease and infertility. Making matter worse, our current methods for tracking and controlling gonorrhea are actually contributing to the spread of resistant disease.

A SLOW BUT STEADY SPREAD

GONORRHEA is the first of the major sexually transmitted diseases (STDs) to tiptoe to the threshold of untreatability. True, chlamydia, which infects 426 of every 100,000 people in the country every year, is more common, and cases of syphilis, which doubled in incidence between 2000 and 2010, are growing faster. But syphilis infects only 4.5 of every 100,000 people, and neither chlamydia nor syphilis has developed significant resistance to antibiotics.

Gonorrhea, in contrast, has been developing defenses against drug treatment for decades. The latest news from Japan and California is making the disease a priority for public health planners—a status it has not known since before Alexander Fleming and the discovery of penicillin. Once antibiotics became abundant and inexpensive, gonorrhea and syphilis seemed like solved problems.

Neither infection was vanquished, however. Gonorrhea, in particular, held on by borrowing DNA from other bacteria to construct new microbiological defenses. It steadily gained resistance against entire classes of antibiotics: first the penicillins in the 1960s, then the tetracyclines in the 1980s, and Cipro and its chemical cousins, known as fluoroquinolones, in the 1990s. By 2000 the only class of drugs that could provide what public health strategies rely on—something that is inexpensive, delivered in a single dose and works well enough to obviate follow-up appointments—was the cephalosporins.

MOVING FROM EAST TO WEST

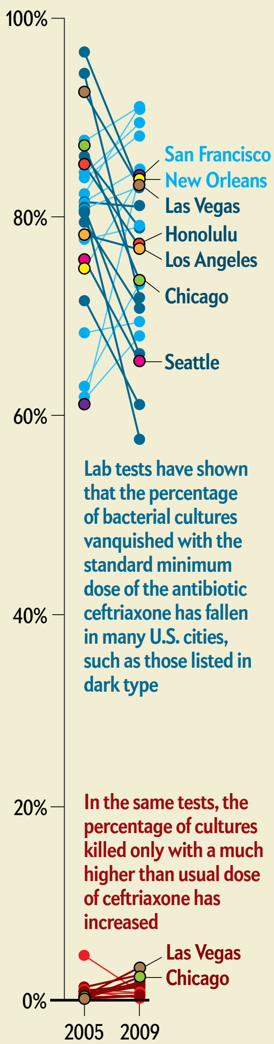
CEPHALOSPORIN RESISTANCE has been emerging in Japan, and moving east and west from there, for at least a decade. In 1999 physicians in Kitakyushu in southern Japan saw two men with gonorrheal infections that had not responded to the usual doses of cephalosporins or related drugs. Within two years more resistant cases emerged. A clinic in Hawaii treated a man with the standard dose of cefixime—a cephalosporin that comes in oral form—but he returned because his symptoms had not gone away. The man said he had had two sex partners who came from Japan, both women. One woman could not be found; the other woman and the man were cured only after receiving higher than usual doses of several different drugs.

Rapid international travel allowed the resistance mutation to hopscotch the globe. Sweden found its first case of the less susceptible strain in 2002. By 2005 it was in England. In 2010 Norway identified its first cases, in men who had had sex with women while traveling in the Philippines and Spain. That same year a Swedish man who contracted gonorrhea after having sex with a woman in Japan could not be cured until he received four times the standard dose of ceftriaxone, an injectable cephalosporin that doctors used because oral cefixime no longer worked. "We may now be reaching the ceftriaxone [doses] for which complete bacterial eradication … will be impossible," warned the physicians who treated him in a February 2011 report.

Last July Japanese researchers announced at a meeting in Canada that they had found a gonorrhea strain in a Kyoto sex worker that was "highly resistant" to both ceftriaxone "and most other antimicrobials tested." The infection was finally controlled with intravenous antibiotics, but experts say that was a one-time fix, impractical for most clinics. In March other researchers announced a similar case in France.

"We can't go back to older antibiotics," says Peter Leone, who is board chair of the National Coalition of STD Directors and medical director of North Carolina's STD prevention program. "Once resistance emerges in gonorrhea, it is there for good. Cephalosporins are all we have left."

Disturbing Gonorrhea Data



BAD NEWS: Bold lines reveal two worrying trends: fewer susceptible strains of gonorrhea and a growing number of resistant strains.

SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION

UNCERTAIN WHAT COMES NEXT

EFFORTS TO CONTROL STDs may have inadvertently accelerated the spread of resistance. For years standard practice has been to quickly identify an infection, dole out the appropriate treatment and then move on to the next patient. If symptoms return, the assumption has been that the patient was reinfected. Experts now say that such patients may in fact have harbored resistant bacteria that were never killed in the first place—bacteria that the patients possibly spread to others.

Physicians would not have recognized that they were dealing with increasingly resistant bacteria, because the rapid tests most commonly used to diagnose sexual infections cannot identify resistant organisms. Instead the tests look for a DNA segment that is unique to gonorrhea, destroying the bacteria in the process. Identifying resistance requires intact living bacteria that researchers can grow in a lab dish and expose to antibiotics to see which drugs work or do not.

Routinely testing patients for resistant strains with the culture tests instead of rapid tests would be costly and time-consuming. But in the February *New England Journal* editorial, lead author Gail Bolan, director of the CDC's division of STD prevention, argues that it is necessary. She also recommends retesting patients after treatment to make sure the infection is gone.

Doctors who treat sexually transmitted infections say that although such changes are sensible, they are not easy. Collecting bacterial samples for analysis requires supplies that most offices do not keep on hand, says Melanie Thompson, executive director of the AIDS Research Consortium of Atlanta, which also does STD testing. "A health care provider who suspected a resistant case would have to recognize it," she explains, "contact the CDC or state health department to report it, go about getting the materials and then get the patient back in to give a sample."

Barry, who helped to reveal that cephalosporins are becoming unreliable and now works for the California Department of Public Health, says the news of burgeoning resistance has not reached either patients or most frontline physicians. "We need to make clinicians aware of the problem and to make patients aware that it is not normal for symptoms to come back," he says.

For any infectious disease, the ultimate control strategy is vaccination, but so far attempts to create a vaccine against gonorrhea have failed. Meanwhile, although infectious disease experts strongly encourage research into new antibiotics for gonorrhea, only one clinical trial is under way, and it is investigating combinations of older drugs, not new compounds. Some older drugs, such as azithromycin, have already started losing effectiveness against gonorrhea bacteria.

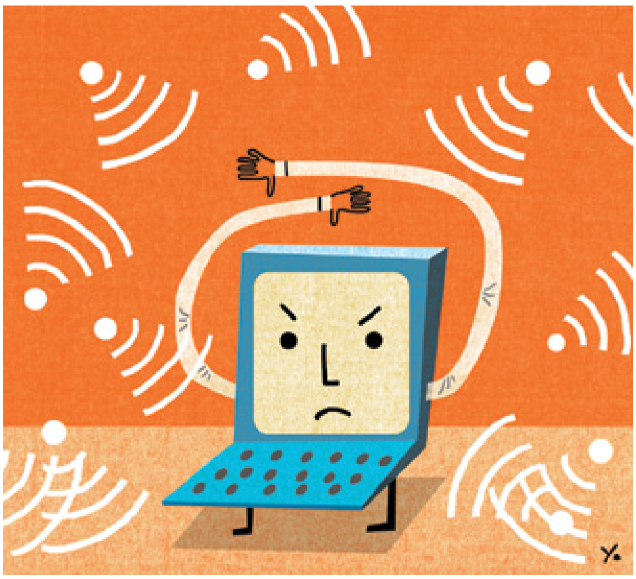
All these efforts—to educate physicians and patients, to track resistant strains and to develop new treatments—must be carefully targeted and well coordinated with one another. If not, truly untreatable gonorrhea, and its expensive, destructive consequences, could be the worldwide result. SA

Graphic by Jen Christiansen

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

The Trouble with Wi-Fi

Impossible connections, dropped signals, phantom networks—why wireless Internet still seems stuck in the Stone Age



To most people, Wi-Fi is something of a miracle. Within 150 feet of some hidden base station, your laptop, tablet or phone can get online at cable-modem speeds—wirelessly.

But Wi-Fi is also something of a mystery. So many readers ask me about Wi-Fi that I've hunted down the answers, once and for all, from the nation's most expert experts.

Often my laptop detects a four-bar Wi-Fi hot spot, but I can't get online. What gives?

In the mid-1990s Alex Hills built a huge wireless network at Carnegie Mellon University that became the prototype for modern Wi-Fi networks—a story he tells in his book *Wi-Fi and the Bad Boys of Radio*. I figured that he would be perfect for this one. His explanation:

"Two issues might cause this. First, radio problems. The bars are an indication of how strong the Wi-Fi signal is, but they don't tell you anything about interference or other radio problems that can corrupt a strong signal.

"Second, most Wi-Fi systems connect to wired networks that connect you to the Internet. But there may be problems in these wired networks: problems with link speeds, switches, routers, servers, and the like. You have a good Internet connection only when all of the links in the chain are doing their jobs."

Why do expensive hotels charge for Wi-Fi but inexpensive hotels don't?

Don Millman's company, Point of Presence Technologies, runs the Wi-Fi for 150 hotels. His answer:

"Expense accounts: higher-end hotels attract business travelers who expense their stays, so the fee matters less to them."

We're frequently warned about the hazards of using free open hot spots, like the ones at coffee shops. What, exactly, is the risk?

Glenn Fleischman has covered networking for more than a decade (currently on the *Economist*'s Babbage blog):

"A bad guy across the room might be running free software that sniffs every bit passing over the wireless network and grabs passwords, credit card numbers, and the like.

"You don't have to worry about banking and e-commerce Web sites; they're protected by secure, encrypted connections.

"But without encrypting your e-mail and regular Web sessions, you never know if someone sitting within 'earshot' is slurping down your data for the purposes of identity theft or draining a bank account. My tip: always use a virtual private network (VPN) connection, which blocks anyone on the local network from seeing anything but scrambled data."

What's up with the "Free Public Wi-Fi" hot spot that sometimes shows up at hotels and airports—even on planes—but that rarely yields any actual connection?

I'll field this one: Don't bother trying to connect to "Free Public Wi-Fi" (or "hpsetup" or "linksys"). It's never a working Wi-Fi hot spot. It's actually a viral "feature" of Windows XP running amok.

Whenever Windows XP connects to Wi-Fi, it also broadcasts that hot spot's name to other computers as an "ad hoc" (PC-to-PC) network so that they can enjoy the connection, too. Someone, somewhere, once created a real hot spot called Free Public Wi-Fi, probably as a prank. Ever since, that name has been broadcast wirelessly from one Windows computer to another. (Macs see the phony hot spot, too, but don't rebroadcast it.)

In public places, people try and fail to connect—but now *their* PCs start rebroadcasting this ad hoc network's name, too, and on and on it goes. Best bet: don't connect. SA

SCIENTIFIC AMERICAN ONLINE
More Wi-Fi questions answered: ScientificAmerican.com/may2012/pogue

Illustration by James Yang

QUANTUM PHYSICS

LOOPS, TREES AND THE SEARCH FOR NEW PHYSICS

Maybe unifying the forces of nature isn't quite as hard as physicists thought it would be

By Zvi Bern, Lance J. Dixon and David A. Kosower

Illustration by Kenn Brown and Chris Wren, Mondolithic Studios

Zvi Bern is a physics professor at the University of California, Los Angeles. He recently co-organized a three-month workshop at the Kavli Institute for Theoretical Physics at U.C. Santa Barbara to discuss high-energy particle scattering. The eldest of his three children is a physics major at Brandeis University. The other two are still trying to decide whether their father's profession is cool.

Lance J. Dixon remembers getting interested in science when he watched the launch of Pioneer 10, the first space probe to visit the outer solar system. Today he is a professor at the SLAC National Accelerator Laboratory. He spent the last academic year at CERN near Geneva, talking with experimenters about how to best use the new theoretical predictions described in this article.

David A. Kosower is as passionate about science as he is about traveling, skiing and running. He is a senior scientist at the Institute of Theoretical Physics at the French Alternative Energies and Atomic Energy Commission's Saclay research center. He is a current holder of a European Research Council Advanced Grant.

ON A SUNNY SPRING DAY

one of us (Dixon) entered the London Underground at the Mile End station on his way to Heathrow Airport. Eyeing a stranger, one of more than three million daily passengers on the Tube, he idly wondered: What is the probability the stranger would emerge at, say, Wimbledon? How could you ever figure that out, given that the person could take any number of routes? As he thought about it, he realized that the question was similar to the knotty problems that face particle physicists who seek to make predictions for particle collisions in modern experiments.

The Large Hadron Collider (LHC) at CERN near Geneva, the premier discovery machine of our age, smashes together protons traveling at nearly the speed of light to study the debris from their collisions. Building the collider and its detectors pushed technology to its limits. Interpreting what the detectors see is an equally great, if less visible, challenge. At first glance, that seems rather strange. The Standard Model of elementary particles is well established, and theorists routinely apply it to predict the outcomes of experiments. To do so, we rely on a calculational technique developed more than 60 years ago by the renowned physicist Richard Feynman. Every particle physicist learns Feynman's technique in graduate school. Every book and magazine article about particle physics for the public is based on Feynman's concepts.

Yet his technique has become obsolete for state-of-the-art problems. It provides an intuitive, approximate way to grasp the very simplest processes but is hopelessly laborious for more complicated ones or for high-precision calculations. Predicting what will emerge from a particle collision is even more daunting than predicting where a subway passenger will go. All the computers in the world working together would be unable to determine the outcome of even a fairly common collision at the LHC. If theorists cannot make precise predictions for known laws of physics and known forms of matter, what hope do we have of telling when the collider has seen something truly new? For all we know, the LHC may already have found answers to some of the greatest mysteries of nature, and we remain in the dark just because we cannot solve the equations of the Standard Model accurately enough.

In recent years the three of us and our colleagues have developed a new way of analyzing particle processes that bypasses the complexity of Feynman's technique. Called the unitarity method, it amounts to a highly economical way of predicting what a subway passenger will do by realizing that the passenger's options at

IN BRIEF

Recently a silent revolution has swept through physicists' understanding of particle collisions. The concepts introduced by the iconic physicist Richard Feynman have reached the limit of their usefulness for many applications, and the authors and their colleagues have developed a fresh approach.

Using it, physicists can describe more reliably how ordinary particles behave under the extreme conditions at the Large Hadron Collider at CERN, aiding experimentalists in their search for exotic particles and forces.

More profoundly, the novel methods breathe new life into a unified theory that physicists left for dead in the 1980s. The force of gravity looks like two copies of the strong subnuclear interactions working in unison.

each decision point are actually rather limited and can be broken down into probabilities for sequences of actions. Many theoretical problems in particle physics that were intractable have been cracked wide open by the new idea. Their solutions allow us to understand in unprecedented detail what our current theory of nature predicts so that we will know a new discovery when we see it. The method has also produced a wealth of results for an idealized cousin of the Standard Model that is of special interest to physicists as a stepping-stone to the ultimate theory of nature.

The unitarity approach is more than a helpful calculational trick. It suggests a radical new vision of theories of particle interactions governed by unexpected symmetries, reflecting an underappreciated elegance of the Standard Model. Notably, it has revealed a strange twist in the decades-old effort to unite quantum theory and Einstein's general theory of relativity into a quantum theory of gravity. Up until the 1970s, physicists assumed that gravity behaves like the other forces of nature and sought to extend our existing theories to cover it. When they applied Feynman's technique, however, they either got nonsensical results or were stymied by the math. Gravity, it seemed, was not like the other forces after all. Discouraged, physicists turned to more revolutionary ideas such as supersymmetry and, later, string theory.

The unitarity method, however, has allowed us to actually do calculations that were contemplated in the 1980s but seemed hopelessly beyond reach then. We have found that some of the supposed inconsistencies are in fact absent. Gravity *does* look like the other forces, albeit in an unexpected way—it behaves like a "double copy" of the strong subnuclear force that binds the constituents of nuclei together. The strong force is transmitted by particles known as gluons; gravity should be transmitted by particles known as gravitons. The new picture is that each graviton behaves like two gluons stitched together. This concept is quite strange, and even experts do not yet have a good mental image of what it means. Nevertheless, the double-copy property provides a fresh perspective on how gravity might be unified with the other known forces.

FROM TREES TO THICKETS

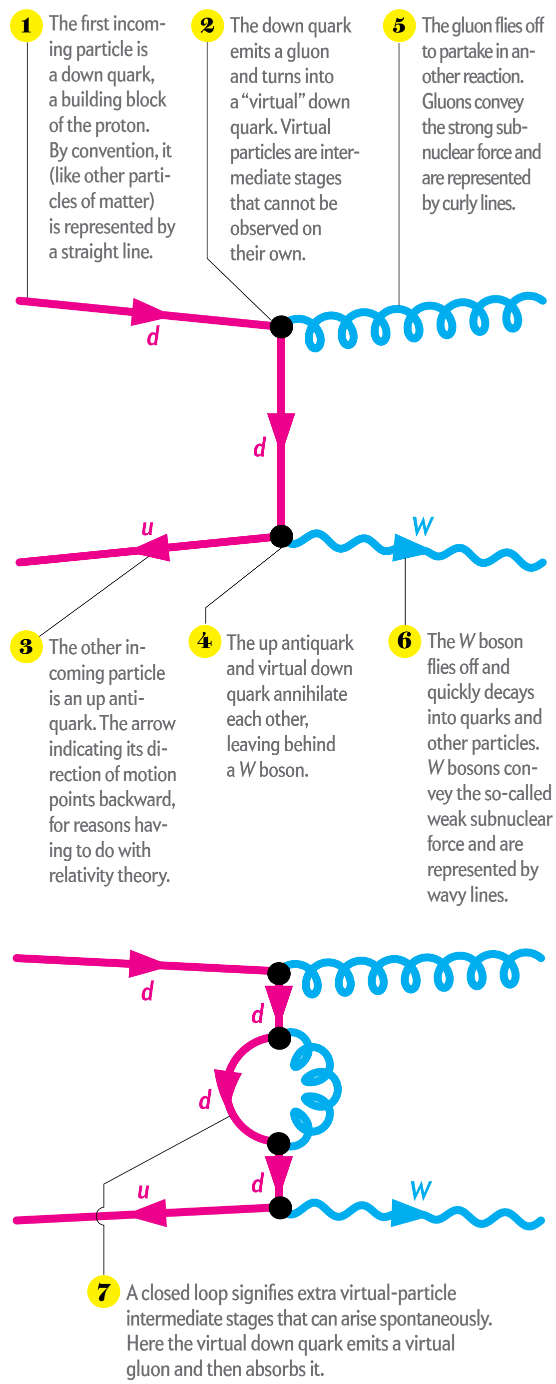
WHAT MADE FEYNMAN'S TECHNIQUE so compelling and useful is that it gives a precise graphical recipe for extremely complicated calculations. It is based on diagrams that give a visual picture of two or more particles colliding or scattering off one another. At every research institution studying elementary particle physics, you can find blackboards covered by these diagrams. To make quantitative predictions, a theorist draws a set of diagrams, each representing one of the conceivable ways a collision may unfold; it is analogous to one of the possible routes an Underground rider might take. Following a set of detailed instructions that Feynman and his colleagues, notably Freeman Dyson, laid down, the theorist then assigns a number to each diagram, giving the probability the event will take place in that way.

The downside is that the number of diagrams one can draw is enormous—in principle, infinite. In the applications for which Feynman originally developed his rules, this disadvantage did not matter. He was studying quantum electrodynamics (QED), which describes how electrons interact with photons. The interaction is governed by a quantity, the coupling, approximately equal to $1/137$. The smallness of the coupling ensures that complicated diagrams receive a low weighting in the calculation and can often be ignored altogether. That is like saying that an Un-

ANATOMY OF A FEYNMAN DIAGRAM

When Particles Collide

All around us all the time, elementary particles are attracting, repelling, hitting, mutating or annihilating one another. To visualize the quantum hurly-burly, Nobelist Richard Feynman created a system of stick-figure-like diagrams. Those below depict two quarks interacting to give birth to a gluon and *W* boson.



Graphics by Zvi Bern, Lance J. Dixon, David A. Kosower and Harald Ita derground rider is usually better off taking a fairly simple route.

Two decades later physicists extended Feynman's technique to the strong subnuclear force. By analogy with QED, the theory of the strong force is known as quantum chromodynamics (QCD). QCD is also governed by a coupling, but as the word "strong" suggests, its value is higher than that of the electromagnetic coupling. On the face of it, a larger coupling increases the number of complicated diagrams that theorists must include in their calculations—like an Underground rider who is willing to take very circuitous routes, making it hard to predict what he or she will do. Fortunately, at very short distances, including the distances relevant for collisions at the LHC, the coupling diminishes in value and, for the very simplest collisions, theorists can again get away with considering only uncomplicated Feynman diagrams.

For messy collisions, though, the full complexity of the Feynman technique comes rushing in. Feynman diagrams are classified by the number of external lines and the number of closed loops they have [*see box at left*]. Loops represent one of the quintessential features of quantum theory: virtual particles. Though not directly observable, virtual particles have a measurable effect on the strength of forces. They obey all the usual laws of nature, such as the conservation of energy and of momentum, with one caveat: their mass can differ from that of the corresponding "real" (that is, directly observed) particles. Loops represent their ephemeral life cycle: they pop into existence, move a short distance, then vanish again. Their mass determines their life expectancy: the heavier they are, the shorter they live.

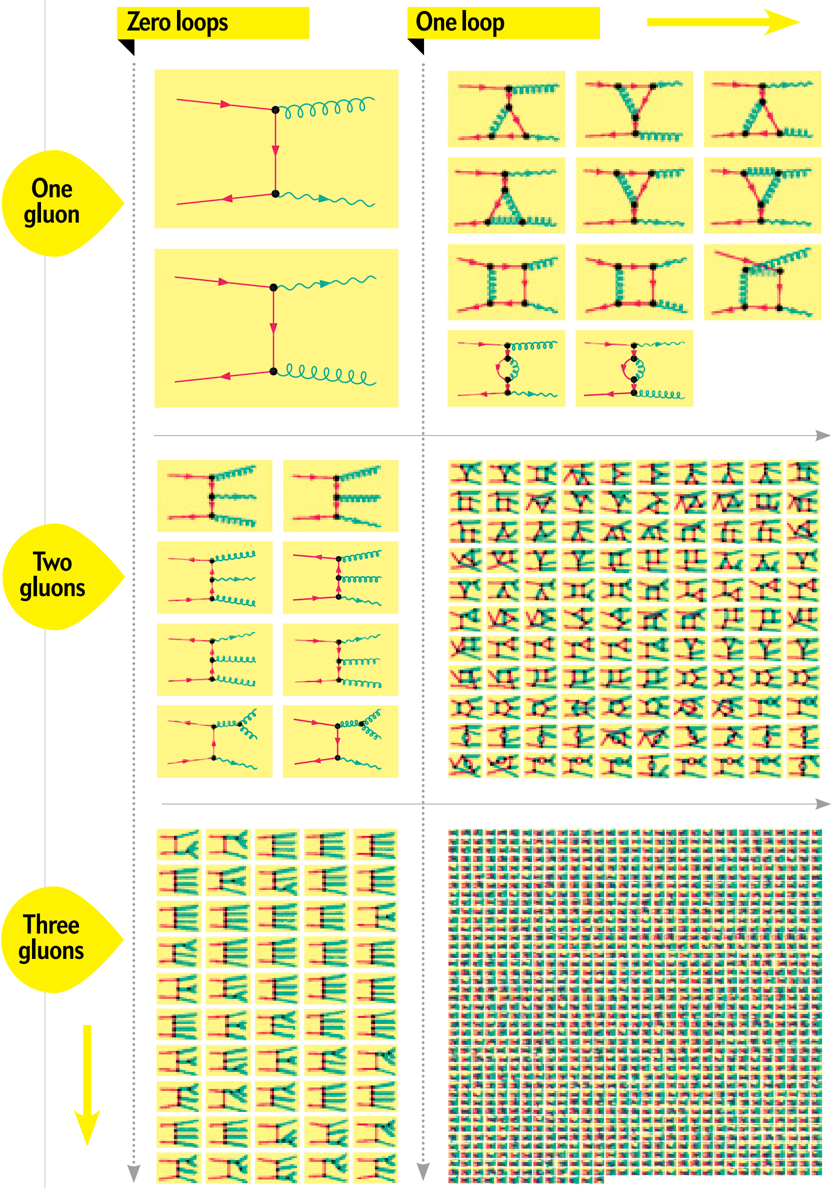
The simplest Feynman diagrams ignore virtual particles; they have no closed loops and are called tree diagrams. In quantum electrodynamics, the simplest diagram of all shows two electrons repelling each other by exchanging a photon. Progressively more complicated diagrams add loops one by one. Physicists refer to this additive procedure as "perturbative," meaning that we start with some approximate estimate (represented by the tree diagrams) and gradually perturb it by adding refinements (the loops). For instance, as the photon travels between the two electrons, it can spontaneously split into a virtual electron and virtual antielectron, which live a short while before annihilating each other, producing a photon. The photon resumes the journey the original photon had been taking. In the next level of complexity, the electron and antielectron might themselves split temporarily. With increasing numbers of virtual particles, the diagrams describe quantum effects with increasing precision.

Even tree diagrams can be challenging. In the case of QCD, if you were brave enough to consider a collision involving two incoming and eight outgoing gluons, you would need to write down 10 million tree diagrams and calculate a probability for each. An approach called recursion, pioneered in the 1980s by Frits Berends of Leiden University in the Netherlands and Walter Giele, now at Fermilab, tamed the problem for tree diagrams but had no obvious extension to loops. Worse, closed loops make the workload overwhelming. Even a single loop causes an explosion in both the number of diagrams and the

WHY FEYNMAN DIAGRAMS DRIVE PHYSICISTS MAD

Too Many to Keep Track Of

Each Feynman diagram provides an intuitive way to visualize one possible way that particles might interact. The trouble is that there are countless other ways, too. A quark-quark interaction might produce more than one gluon or involve more than one virtual-particle loop, or both. The calculations quickly become unmanageable.



complexity of each. The mathematical formulas could fill an encyclopedia. Brute force—harnessing the power of an ever growing number of computers—can fight off the tide of complexity for a while but soon succumbs to increasing numbers of external particles or loops.

QUANTUM FLUCTUATIONS OF SPACE AND TIME ARE MUCH MORE INNOCUOUS THAN WE IMAGINED.

Even worse, what started as a concrete way to visualize the microscopic world can cloak it in obscurity. Individual Feynman diagrams are often impenetrably baroque, and when we have to juggle so many of them, we lose track of the essential physics. What is astounding is that the final result, found by summing up all the diagrams, can be quite simple. Different diagrams partially negate one another, and sometimes formulas with millions of terms collapse down to a single term. These cancellations suggest that the diagrams are the wrong tools for the job—like trying to pound in a nail with a feather. There must be a better way.

BEYOND FEYNMAN DIAGRAMS

OVER THE YEARS physicists tried out many new techniques to do calculations, each slightly better than the one before it, and gradually the outlines of an alternative to Feynman diagrams took shape. Our own involvement began in the early 1990s, when two of us (Bern and Kosower) showed how string theory could simplify QCD calculations by summarizing all the relevant Feynman diagrams with a single formula. With this formula, the three of us analyzed a particle reaction that had never been understood in detail before: the scattering of two gluons into three gluons, with one virtual-particle loop. This process was very complicated by the standards of the time but could be fully described by an amazingly simple formula, which fit on a single page.

The formula was so simple that, together with David Dunbar, who was at the University of California, Los Angeles, at the time, we found we could understand the scattering almost entirely in terms of a principle called unitarity. Unitarity is the requirement that the probabilities of all possible outcomes add up to 100 percent. (Technically the quantities are not probabilities but square roots of probabilities, but this distinction is not so important here.) Unitarity is implicit in Feynman's technique but tends to be hidden by the complexity of the calculations. So we developed an alternative technique that put it front and center. The idea of basing calculations on unitarity had come up in the 1960s [see "Strongly Interacting Particles," by Geoffrey F. Chew, Murray Gell-Mann and Arthur H. Rosenfeld; SCIENTIFIC AMERICAN, February 1964], although it fell out of favor. As repeatedly happens in science, discarded ideas can come roaring back in a new guise.

The key to the success of the unitarity method is that it avoids the direct use of virtual particles, which are the prime reason that Feynman diagrams get so complicated. Such particles have both real and spurious effects. By definition, the latter *have* to cancel out of the final result, so they are excess mathematical baggage that physicists are happy to leave behind.

The method can be understood by analogy to a complicated subway system like the London Underground, with multiple paths between any two subway stations. Suppose we want to know the probability that a person entering at Mile End leaves at Wimbledon. The Feynman technique adds up the probabilities of all conceivable paths. All really means *all:* besides the paths through corridors and tunnels, Feynman diagrams include paths through solid rock where there are no subway lines or walkways. Those unrealistic paths are the analogues of the spurious contributions from virtual-particle loops. They cancel out in the end, but in the intermediate stages of the calculation, we need to keep track of them all. In the unitarity approach, we consider only paths that make sense. We calculate the probability that a person takes a particular route by subdividing the problem: What is the probability the person goes through a particular turnstile, one pathway or another one, at each step of the journey? This procedure greatly cuts down the size of calculations.

The choice between the Feynman and unitarity methods is not a matter of right and wrong. Both express the same basic physical principles. Both would eventually lead to the same numerical probabilities. But they represent different levels of description. A single Feynman diagram, out of the tens of thousands for a messy collision, is like a single molecule within a droplet of fluid. In principle, you can determine what a fluid will do by tracking all the individual molecules, but that makes sense only for a microscopically small droplet. It is not only cumbersome but also unenlightening. The fluid could be cascading down a hill, but you would scarcely know that from the molecular description. You are better off considering higher-level properties such as fluid velocity, density and pressure. Likewise, instead of viewing a particle collision as built up one by one from individual Feynman diagrams, physicists can think of it holistically. We concentrate on the properties that govern the process as a whole—unitarity, as well as special symmetries that the unitarity method gives prominence to. In special cases, we can make theoretical predictions with perfect precision, which would take infinitely many diagrams and an infinite amount of time with Feynman's technique.

The advantages go even further. After we developed the unitarity method for virtual-particle loops, another team, then at the Institute for Advanced Study in Princeton, N.J.—Ruth Britto, Freddy Cachazo, Bo Feng and Edward Witten—added a complementary twist. They thought about tree diagrams again and computed the probability of a collision involving, say, five particles in terms of the probability of a collision of four particles, followed by one particle splitting into two. That is a stunning conclusion because a five-particle collision usually looks very different from these two sequential collisions. In more ways than one, we can subdivide daunting particle problems into simpler pieces.

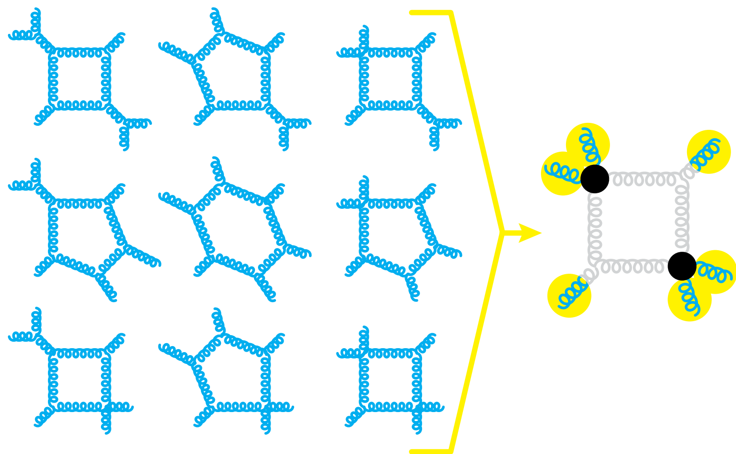
SMASHING WATCHES

PROTON COLLISIONS at the LHC are exceptionally complex. Feynman himself once compared them to figuring out how Swiss watches work by smashing them together, and his technique struggles to track what goes on during them. Protons are not elementary particles but little balls of quarks and gluons bound together by the strong subnuclear force. When they slam together, quarks can bounce off quarks, quarks off gluons, gluons off gluons. Quarks and gluons can split into still more quarks and gluons. They ultimately clump together in composite parti-

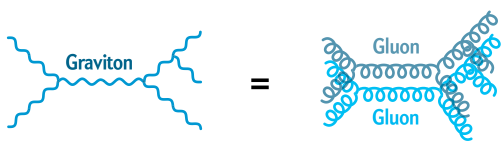
A BETTER WAY

Making Life Simpler

The authors have developed an alternative to Feynman diagrams called the unitary method. It exploits basic principles in quantum theory to consolidate multiple Feynman diagrams, making calculations possible that were once intractable.



The technique has revealed features of the natural world that were implicit in current theories but got lost in the swarms of Feynman diagrams. Most striking among them is a possible way to incorporate the force of gravity, which has resisted past efforts to explain it. The particles that transmit the force of gravity, known as gravitons, bear a remarkable similarity to gluons; in fact, mathematically, each graviton is like two copies of a gluon, working together like contestants in a three-legged race.



cles that shoot out of the collider in narrow sprays that physicists call jets.

Somewhere buried in that mess may be things that human beings have never seen before: new particles, new symmetries, maybe even new dimensions of spacetime. But sifting them out will be tough. To our instruments, exotic particles look rather like ordinary ones. The differences are small and easily missed. With the unitarity method, we can describe ordinary physics so precisely that extraordinary physics will stand out.

For instance, Joe Incandela of U.C. Santa Barbara, who is currently the spokesperson for the 2,000-plus-physicist CMS experiment at the LHC, came to us with a question about his team's search for exotic particles that make up cosmic dark matter, the mysterious stuff that astronomers think is out there but that physicists have yet to identify. Any such particles the LHC produces would elude the CMS detector, leaving the impression that some energy had gone missing. Unfortunately, an apparent loss of energy does not, in itself, mean that the LHC has synthesized dark matter. For instance, the LHC frequently produces an ordinary particle called the *Z* boson, and one fifth of the time it decays into two neutrinos, which also interact very weakly and escape the detector without registering. How could one predict the number of Standard Model particles whose effects mimic dark particles?

Incandela's group proposed a solution: take the number of photons the CMS detector records, extrapolate to the number of events involving neutrinos and see whether they fully explain the apparent energy loss. If not, the LHC might be creating dark matter. This idea typifies the indirect estimates experimental physicists are always having to make because they lack the ability to observe certain types of particles directly. But to pull it off, Incandela's group needed to know precisely how the number of photons related to the number of neutrinos. Unless the precision was high enough, the backdoor strategy would fail. With several colleagues, we studied the problem using the new theoretical tools and were able to assure Incandela that the precision was sufficiently high. Reassured, the CMS team applied its technique and set stringent constraints on dark matter particles. Our technique had proved its worth.

This success has inspired us to push forward with more ambitious calculations. As is common in modern particle physics, we work with collaborators worldwide, including Fernando Febres Cordero of Simón Bolívar University in Caracas, Venezuela, Harald Ita of Tel Aviv University and U.C.L.A., Daniel Maître of Durham University in England, Stefan Höche of SLAC and Kemal Ozeren of U.C.L.A. Together we made precise predictions for the probability that LHC collisions would produce a pair of neutrinos along with four jets. Using Feynman diagrams, these calculations would have been too imposing even for a large team of physicists working hard for a decade assisted by state-of-the-art computers. The unitarity method let us do them in less than a year. To our delight, another LHC team, the ATLAS collaboration, has already compared our predictions with its data, and the results are in excellent agreement so far. Going forward, experimenters will use these results to search for new physics.

The unitarity method has also aided the search for the long-sought Higgs particle. A sign of the Higgs is the production of a single electron, a pair of jets and a neutrino, the neutrino again leaving the impression that energy has gone missing. The same outcome can also arise from particle reactions not involving the Higgs. One of our first uses of the unitarity method was to calculate the precise probability of these confounding reactions.

BACK TO GRAVITY

AN EVEN MORE IMPRESSIVE USE of the unitarity method is to study quantum gravity. For physicists to develop a fully consistent theory of nature, we must find a way to fit gravity into a quantum-mechanical framework. If gravity behaves like the other forces of nature, it should be transmitted by graviton particles. Gravitons would collide and scatter just as other particles do, and we could draw Feynman diagrams for them. Yet attempts in the mid-1980s to describe graviton scattering by quantizing Einstein's theory in the simplest possible way led to nonsensical predictions, such as infinite values for quantities that should clearly be finite. Infinite quantities, per se, are not the problem. They can arise at intermediate stages of calculations even in a well-behaved theory such as the Standard Model, but they should cancel out of any quantity that is potentially measurable. For gravity, no such cancellations appeared to occur. In concrete terms, it means that the quantum fluctuations of space and time, dubbed "spacetime foam" by the late quantum gravity pioneer John Wheeler, spiral out of control.

One possible explanation is that nature contains undiscovered particles that rein in these quantum effects. This idea, embodied in so-called supergravity theories, was studied intensively during the 1970s and early 1980s [see "Supergravity and the Unification of the Laws of Physics," by Daniel Z. Freedman and Peter van Nieuwenhuizen; Scientific American, February 1978]. But the excitement died down when indirect arguments suggested that nonsensical infinities would still arise with three or more virtual-particle loops. It seemed that supergravity was doomed to failure.

This disappointment led many to pursue string theory. String theory is a radical departure from the Standard Model. According to it, particles such as quarks, gluons and gravitons are no longer tiny points but oscillations of one-dimensional strings. Particle interactions are spread out over the strings rather than concentrated at a single point, preventing infinities automatically. On the other hand, string theory has encountered its own troubles; for instance, it does not make definitive theoretical predictions for observable phenomena.

DOUBLE TROUBLE

In the mid-1990s Stephen Hawking of the University of Cambridge advocated giving supergravity theories another look. He pointed out that the 1980s-era studies had taken shortcuts that made their conclusions questionable. But Hawking was unable to convince anyone else because there was a good reason that people had taken those shortcuts: the full calculations were hopelessly beyond the capacities of even the most brilliant math whiz. To know for sure whether a Feynman diagram with three virtual-graviton loops produces infinite quantities, we would need to evaluate 10^{20} terms. By five loops, a diagram spawns 10^{30} terms, roughly one for every atom in an LHC detector. The issue appeared destined for the dustbin of undecidable problems.

The unitarity method has completely changed the situation. Using it, we have conducted a physics version of the Innocence Project and reopened the case against supergravity theory. What would have taken the Feynman technique 10^{20} terms, we can now do with dozens. Together with Radu Roiban of Pennsylvania State University, as well as John Joseph Carrasco and Henrik Johansson, who were then graduate students at U.C.L.A., we found that the 1980s-era speculations were wrong. Quantities that seemed destined to be infinite are in fact finite. Supergravity is not as nonsensical as physicists thought. In concrete terms, it means that quantum fluctuations of space and time are much more innocuous in supergravity than previously imagined. If you ply us with fine wine, you might catch us speculating that some version of it might be the long-sought quantum theory of gravity.

Even more remarkably, three gravitons interact just like two copies of three interacting gluons. This double-copy property appears to persist no matter how many particles are scattering or how many virtual-particle loops are involved. It means that, figuratively speaking, gravity is the square of the strong subnuclear interaction. It will take us a while to translate the mathematics into physical insight and check whether it is true under all conditions. For now the crucial point is that gravity may not be so different from the other forces of nature.

As is common in science, after each debate is settled, another erupts. Immediately after our calculations for three loops, skeptics wondered whether trouble might appear at four loops. As also happens frequently, bottles of wine were bet on the outcome of the calculation: an Italian Barolo against a Napa Valley Chardonnay. When we did the calculation, we found no hints of difficulties, settling at least this debate (and popping a Barolo cork).

Is supergravity theory completely free of infinities? Or does its high degree of symmetry merely curb some of its excesses at a small number of loops? In the latter case, trouble should creep in at five loops; by seven loops, quantum effects should grow strong enough to produce infinities. David Gross of U.C. Santa Barbara has put up a bottle of California Zinfandel if no seven-loop infinities arise. To settle this latest bet, some of us have embarked on new calculations. An absence of seven-loop infinities would astound the skeptics and might finally persuade them that supergravity could be self-consistent. Even if it is, though, the theory does not capture other kinds of effects, called nonperturbative, that are too tiny to be seen in the loop-by-loop approach we have been following. Those effects may still require an even deeper theory to handle, perhaps string theory.

Physicists often like to think of new theories as emerging from the bold brushstrokes of new principles—relativity, quantum mechanics, symmetry. But sometimes those theories emerge from a careful reexamination of the principles we already know. The quiet revolution in our understanding of particle collisions has enabled us to work out the consequences of the Standard Model in remarkable detail, leading to significant improvements in our potential to discover physics beyond it. Even more surprisingly, it is letting us follow the unexplored implications of old physics, including a once neglected path toward unifying gravity with the other known forces. In many ways, the journey to understanding the secrets of how elementary particles scatter has not been like riding the predictable London Underground at all but more like a journey on the Knight Bus of Harry Potter tales, where you never quite know what will happen next. SA

MORE TO EXPLORE

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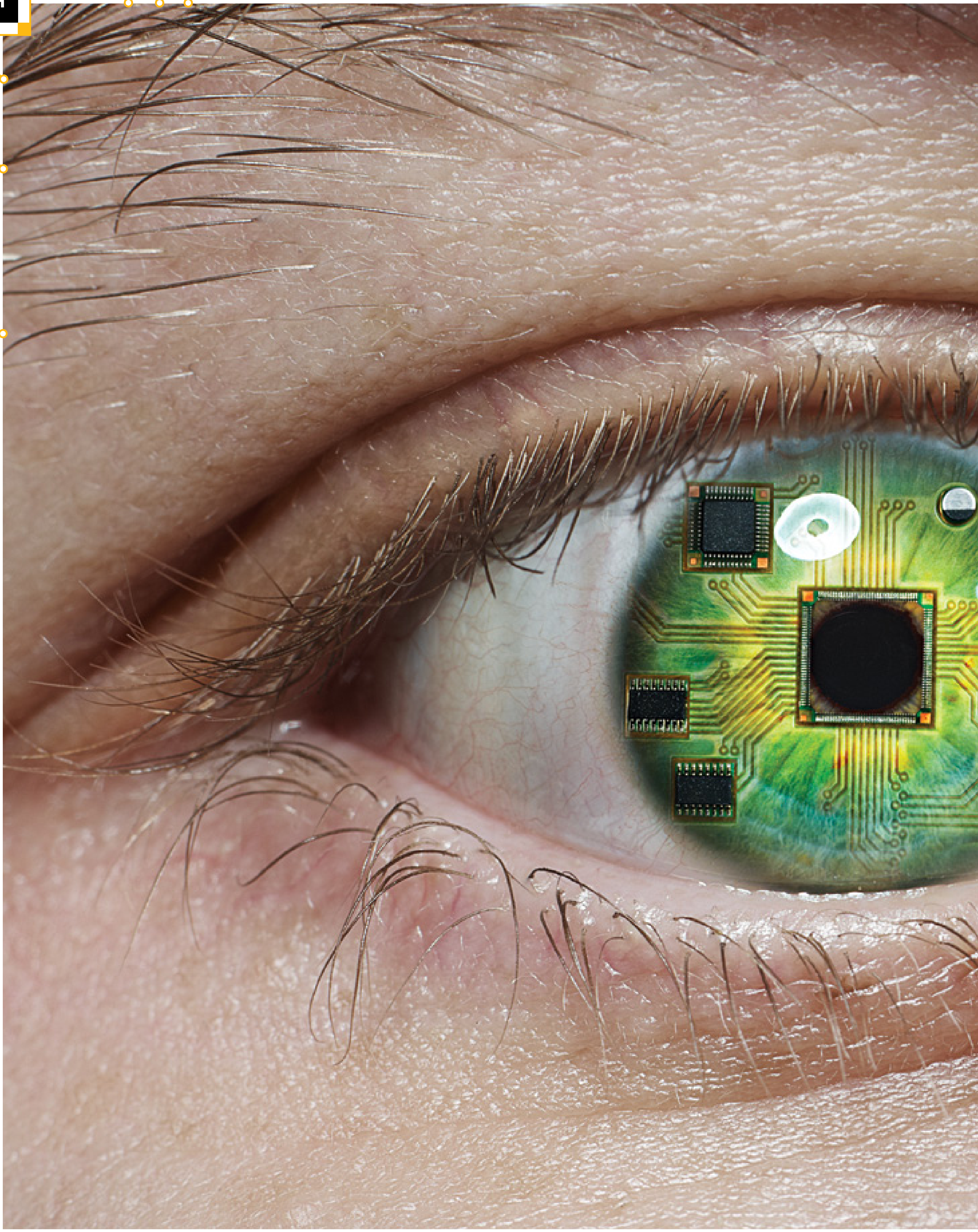
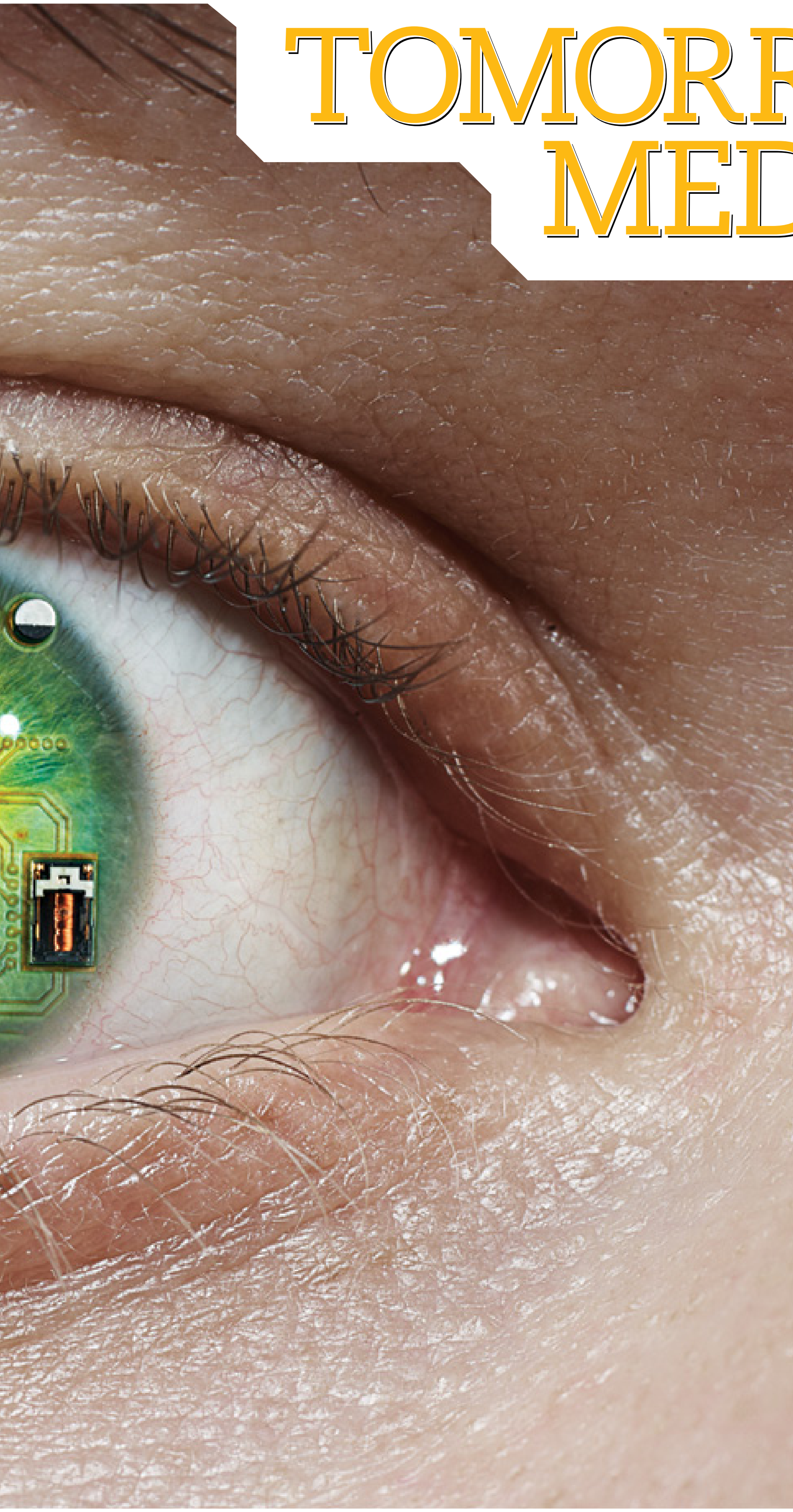
SCIENTIFIC AMERICAN ONLINE
For an animation that shows how the Large Hadron Collider works and how Feynman diagrams explain the outcome, visit **ScientificAmerican.com/may2012/particle**





TOMORROW'S MEDICINE

A look at some of the most promising medical devices now in development

OVER THE PAST FEW YEARS researchers have taken advantage of unprecedented advances in biology, electronics and human genetics to develop an impressive new tool kit for protecting and improving human health. Sophisticated medical technology and complex data analysis are now on the verge of breaking free of their traditional confines in the hospital and computer lab and making their way into our daily lives.

Physicians of the future could use these tools to monitor patients and predict how they will respond to particular treatment plans based on their own unique physiology, rather than on the average response rates of large groups of people in clinical trials. Advances in computer chip miniaturization, bioengineering and material sciences are also laying the groundwork for new devices that can take the place of complex organs such as the eye or pancreas—or at least help them to function better.

The articles on the following pages offer a glimpse at some of the most promising developments in customized technology for genetics, artificial sight, cancer, implantable health monitors and mental illness. Not everything will necessarily pan out. But collectively they suggest that compact medical technology will play an ever increasing role not only in treating the sick but also in safeguarding the health of those who are well. *—The Editors*

Photographs by Dan Saelinger

GENETICS

PERSONALIZED MEDICINE

The cost of sequencing the human genome keeps falling, but making sense of the results remains a challenge

When the Human Genome Project was launched more than 20 years ago, the effort of printing out the entire instruction book for building a human being was expected to require hundreds of sequencing machines, cost $3 billion and take 15 years. Thirteen years later, in 2003, the first "complete" human genome sequence was announced. But that momentous achievement was still a work in progress. Huge gaps remained in the map of the hereditary material that determines a person's genetic destiny, waiting to be filled in.

Fast-forward to January 2012, at the International Consumer Electronics Show in Las Vegas. There amid the gaming consoles and flat-screen televisions stood a gene sequencer, a sleek white box the size of a desktop printer. Its inventors say that when the device hits the market later this year, it will crank out an individual's complete genetic sequence in just a few hours for $1,000, or the cost equivalent of a nice plasma TV.

For years the $1,000 genome has been held out as the tipping point that will usher in a new era of personalized medicine. At that price point, the readouts are supposed to be cheap enough for ordinary doctors to put them to work treating patients with heart disease, cancer or other illnesses based on their own individual genetic risks and drug sensitivities. As gene sequencers like the one displayed become increasingly available, industry watchers argue that the age of comprehensive genetic testing of the human population has finally dawned.

But some say a widespread rollout of the technology would be premature. "It's not ready," says Aravinda Chakravarti, a professor of genetics at the Johns Hopkins University School of Medicine. Chakravarti worries that the potential benefits of personalized genomic medicine have been overpromoted. People do not realize, he says, that full genetic scans, whether done through a physician or bought online, are close to useless right now as medical tools.

The main problem is that the technology has grown faster than the researchers' ability to understand the results it produces. For example, each individual's genetic readout must be compared with lots and lots of other people's readouts for doctors to understand which genetic patterns are important indicators of disease and which can be safely ignored. In addition, many diseases are caused by rare mutations that have not yet been identified. Finally, the task of simply sorting through the sheer mass of data spit out by a genome scan is daunting. "Generating the sequence now is fast and cheap," says Euan A. Ashley, an assistant professor of cardiology at the Stanford University School of Medicine. "But the analysis? Wow. That's not going to be fast, and that's not going to be cheap."

To demonstrate just how complex the process can be, Ashley and a few other researchers at Stanford and at Harvard University analyzed the genome of their colleague Stephen Quake, a professor of bioengineering. It took them six months to figure out how to do it, even though Quake had already sequenced his genome himself, so they had the raw data they needed.

Quake's family history included several instances of heart disease. Sure enough, the team found that he possessed several genetic variants that have been linked to an increased susceptibility to heart attack. But the genetic analysis produced a few curveballs—including an increased likelihood of a hereditary blood disorder called hemochromatosis, even though no one in Quake's family suffers from the condition. At this point, it is impossible to say whether the unexpected result reflects a true danger or some kind of mistake in the sequencing process—the genetic equivalent of a typographical error.

Despite these glitches, Ashley is optimistic about the potential for individualized DNA readouts to transform medical care, envisioning a day when a person's genome is a standard part of the electronic medical record. So far, however, the few patients who have benefited the most from having large portions of their genome analyzed have had rare diseases with genetic variants that were unusual enough to stand out. For the rest of us, our genome awaits—a tale yet untold. —*Nancy Shute*

ARTIFICIAL SIGHT

BIONIC EYE

Synthetic photoreceptors will restore vision to the blind

Miikka Terho knows the difference between an apple and a banana. He can tell you that one is round and sweet and crunches when you bite it and that the other is long and curved and turns to mush if you let it ripen too long. But if you ask him to tell one fruit from the other without touching, smelling or tasting them, he is at a loss. Terho is completely blind. For three months in 2008, however, he recovered the ability to distinguish an apple and banana by sight thanks to a tiny electronic chip that researchers implanted in his left eye. Though brief, the new technology's initial success has permanently changed the prospects for Terho and many others like him.

Terho, who works for an athletic scholarship organization in Finland, has retinitis pigmentosa, a genetic condition that destroys the light-sensitive cells lining the retina at the back of the eye. He could see just fine until age 16, when his night vision began to fail. In his 20s his ability to see in the day deteriorated as well. By age 35 Terho had lost central vision in both his left and right eyes. By 40 he could perceive only hints of light at the periphery of his vision.

Everything changed in November 2008, when Eberhart Zrenner of the University of Tübingen in Germany embedded the chip in the retina of Terho's eye. The chip replaced damaged photoreceptors (known as rods and cones) in the retina. In a healthy retina, photoreceptors convert light into electrical impulses that eventually reach the brain by traveling through several layers of specialized tissue—one of which is made up of so-called biopolar cells. Each of the chip's 1,500 squares, which are arranged in a grid that measures 0.12 inch by 0.12 inch, contains a photodiode, amplifier and electrode. When light shines on one of the photodiodes, it generates a tiny electric current that is strengthened by the adjacent amplifier and channeled to the electrode, which in turn stimulates the nearest bipolar cell, ultimately sending a signal through the optic nerve to the brain. The more light that shines on a photodiode, the stronger the resulting electric current.

Terho's retinal implant opened a window on the world for him that measured about the size of an eight-inch-square piece of paper held at arm's length. Through that window Terho could make out the basic shapes and outlines of people and objects, especially if the contrast between light and dark colors was strong. The implant did not, however, contain enough electrodes to produce sharp images. In addition, the chip allowed him to perceive only shades of gray rather than color because it could not differentiate different wavelengths of light.

Despite these limitations, the implant dramatically changed how Terho interacted with the world within days after his surgery. For the first time in a decade, he was able to see and name objects like silverware and fruit, read letters in large print, approach people in a room and recognize loved ones. Two other patients who received implants around the same time were able to locate bright objects placed against dark backgrounds.

Zrenner had to remove the chips after three months because the design left the patients vulnerable to skin infection: an external pocket-size battery pack delivered power to the amplifiers in the eye through a small cable threaded into the skin, leaving an open wound. Moreover, users needed to be near a computer that wirelessly controlled the frequency of electrical impulses, as well as such aspects of vision as brightness and contrast.

Since 2008 Zrenner has made his implant safer and more portable. The latest model—which has been placed in 10 people so far—is wireless. Underneath the skin a thin cable runs from an electromagnetic coil behind the ear a short distance to the chip at the back of the eye. Placing another electromagnetic coil housed in a small plastic box on top of the skin near the ear completes an electric circuit, which provides power to the implant. By fiddling with knobs on the outer coil, patients can modify brightness and contrast. To improve the technology further, Zrenner wants to implant three chips next to one another in a single retina so that individuals will have a larger field of view.

Although synthetic photoreceptors should prove helpful for any forms of blindness that result from damaged photoreceptors (namely, retinitis pigmentosa, choroideremia, and some kinds of macular degeneration, such as geographic atrophy), they cannot help people with glaucoma or other conditions that degrade the optic nerve.

Another team has also had Zrenner's level of success in clinical studies. California-based Second Sight has developed a retinal implant—Argus II—that also treats retinitis pigmentosa, albeit with a different approach. Argus II captures images of the world in a tiny camera mounted on a pair of glasses, converts those images to electrical impulses and transmits them to an electrode that sits on the surface of the retina, rather than being embedded in it. In contrast to Zrenner's implant, Argus II does not mimic the normal excitation of the retina by light waves. Instead it produces a patchwork of bright and dark dots that patients must learn to interpret.

Restoring even grayscale vision is expensive. Currently the Argus II setup is priced at $100,000 per eye and—once fully tested and approved—Zrenner's retinal implants are likely to cost at least as much. Zrenner must conduct additional clinical trials before European advisory boards will permit him to instruct other surgeons in the procedure. Argus II has been approved for sale throughout much of Europe but not yet in the U.S. The success of the first clinical trials and the speed at which the technology is improving suggest, however, that retinal implants could be more widely available in just a few years. *—Ferris Jabr*

EARLY DETECTION

ZEROING IN ON CANCER

Bioengineers are developing tiny nanoparticles programmed to detect cancer at its earliest stages

Supersmall particles have the potential to fix some of medicine's biggest problems. So-called nanoparticles, which are on the scale of nanometers (one billionth of a meter), are so tiny that 500 of them could be lined up across the width of a human hair. Scientists are engineering them to do everything from delivering drugs within specific parts of the body to providing more detailed images of internal organs. Now researchers are fine-tuning them to uncover cancer cells wherever they might be hiding.

Standard imaging tools detect tumors once they have grown large enough to see on a scan. Nanoparticles can find a single cancer cell in a sample of 10 million normal cells. Experimental nanomedicine detection for breast cancer, for example, has been able to pinpoint tumors 100 times as small as those that can be seen via mammography in laboratory studies. Nanoparticles that are outfitted with cancer-specific proteins or genetic material can also help doctors distinguish between malignant growths and run-of-the-mill inflammation or benign lesions.

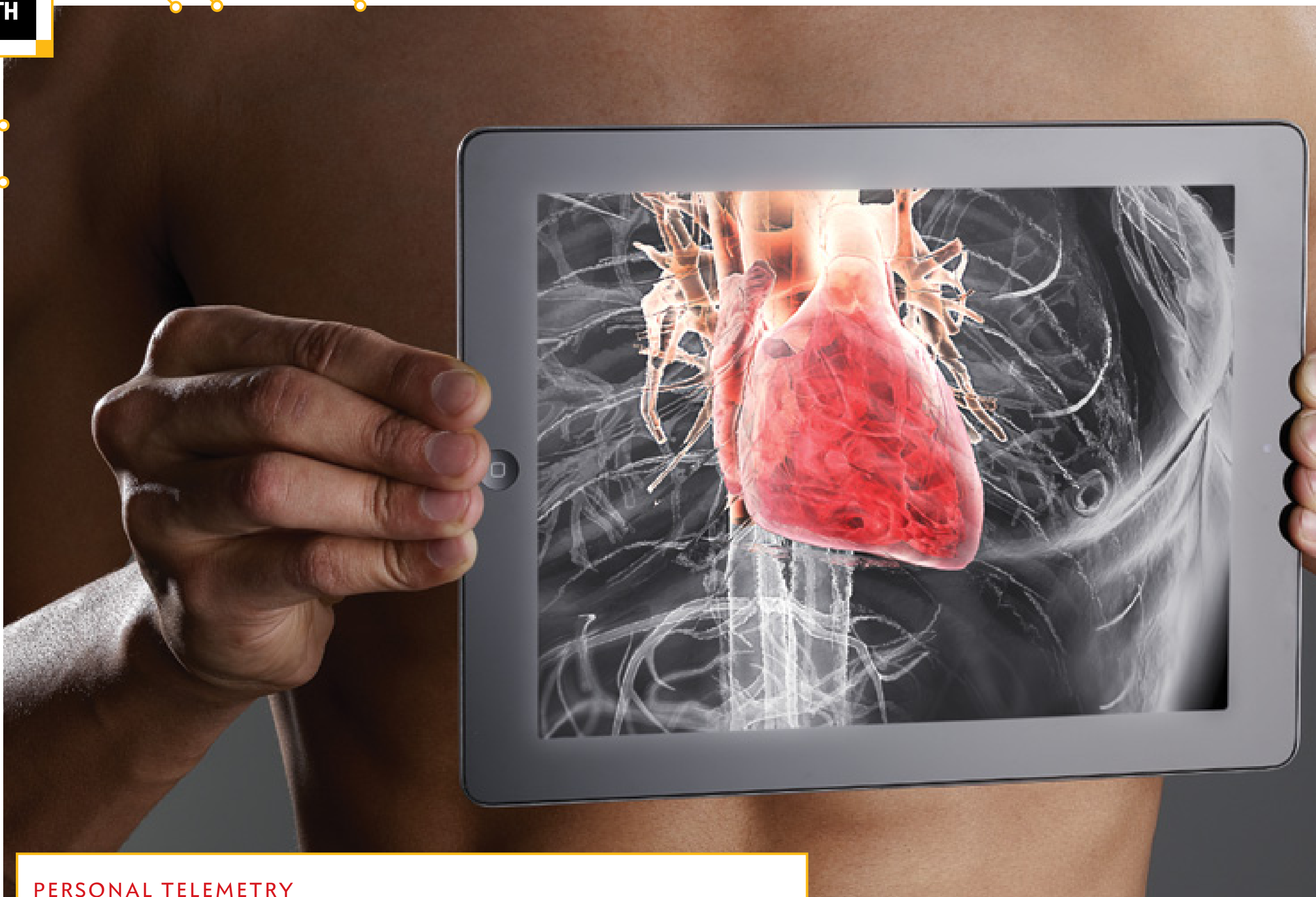
Gregory Lanza, a professor of biomedical engineering at Washington University in St. Louis, and his team are developing nanoparticles that seek out and signal the presence of newly forming blood vessels that specifically feed the growth of tumors—a key stage in the development of colon, breast and other cancers. Such blood vessel growth does not usually occur in noncancerous tissue. This technology could also theoretically inform doctors how quickly a cancer is growing and thus how aggressive treatment should be.

Sanjiv Sam Gambhir, a professor of diagnostic radiology at Stanford University, and his colleagues are focusing on colorectal cancer, trying to find tiny malignancies that a standard colonoscopy might miss. The group is creating nanoparticles made of gold and silica and then adding molecules that instruct the particle to home in on the particular cancer cells. When the targeting molecules attach to a tumor in the colon or rectum, the nanoparticle minerals scatter the light from a specialized endoscope, betraying the presence of the cancer.

Nanoparticle engineers are also attempting to make nanoparticles that perform multiple tasks, such as highlighting tumors in MRI, PET and other scans and even delivering cancer drugs. Such combination nanodevices could allow physicians to see whether a treatment is getting where it is supposed to go—and whether it is working. Even with current targeted therapies that act specifically on cancer cells while sparing normal cells, doctors often do not have a good sense of how much of the medication has reached the tumor. "The imaging component is what allows you to know you actually delivered the drug—and how much," Lanza says.

Efforts to bring nanoparticles to the clinic face some obstacles. Scientists will have to prove, for instance, that these minute helpers are safe for human use. But "the single biggest hurdle" for cancer therapy, Gambhir says, is the lack of plausible targets. Nanoparticles can be quite exquisitely designed, but they "aren't magical," he notes. Researchers do not know enough about the earliest stages of cancer growth to know which molecules the nanoparticles should be directed toward. Without knowing the targets, "we haven't even taken the first step," Lanza says. "We need to walk before we can run." But with the nanomedicine field worldwide projected by various industry analysts to top $130 billion by 2016, the race to find out is on.

—Katherine Harmon



PERSONAL TELEMETRY

SMART IMPLANTABLE DEVICES

New wireless monitors warn patients of an impending heart attack or help them to manage diabetes

Biomedical engineers are developing tiny, implantable monitors that could take some of the guesswork out of how best to treat patients with chronic conditions such as heart disease or diabetes. Several such devices—which send data wirelessly from key regions of the body or the blood to external receivers—are now being tested in the clinic. Eventually implanted monitors could play a more active role in treatment, not solely detecting dangerous arrhythmias, for example, but also jolting a stopped heart back to life. A couple of the instruments that are being developed target two of the most common medical problems:

Heart attacks. Manufactured by Angel Medical Systems in Shrewsbury, N.J., the AngelMed Guardian is roughly the size of a pacemaker and tracks the heart, beat by beat. It is tuned to listen for abnormal patterns, such as a rapid increase in timing or an irregular pulse in people who have recently survived a heart attack (making them at risk for another) but who do not qualify for a pacemaker or implanted cardiac defibrillator. If the device senses another impending attack, it vibrates and causes an external pager to beep and flash, alerting the patient or others to get help. To prevent false alarms, the Guardian needs to detect a problem signal for more than a minute before it sends an alert. These and other cardiac details gleaned from the device can be downloaded wirelessly to a computer for analysis. Angel Medical has licensed its heartbeat-detection technology to a company that makes implanted cardiac defibrillators. The combined technology will allow the device to administer an electric current to the heart if the monitor picks up signs of cardiac arrest or a particularly dangerous arrhythmia, while also sending electrocardiogram results to a physician.

Abnormal glucose levels. A new implantable glucose sensor made by GlySens in San Diego might some day offer millions of diabetics a wireless monitoring system of their own. The device takes near-continuous readings under the skin of a patient's glucose level—which is then correlated to the level in the blood. The result: far more accurate and more complete information for guiding insulin dosing and timing than can be achieved by testing blood from finger pricks. And because the sensor is implanted, it requires less upkeep than current external monitors.

"We want to give the patient and the family a device where they can forget about the device and just have the information," says Joseph Lucisano, a

bioengineer who is also president and chief executive officer of GlySens. "Treatment of diabetes and many other chronic diseases is all about monitoring, recognizing and optimizing patterns of signals," he adds. So having a wireless link that delivers "large volumes of data at minimal cost really will enable a lot of things that we probably can't even anticipate."

Wireless sensors are likely to be even more subtle in the future. Researchers have developed a thin, flexible instrument that can be applied like a temporary tattoo to skin or inside the body and can collect readings on heart rate, muscle contractions and even brain waves. Being developed by mc10, a company in Cambridge, Mass., that creates flexible electronics, the futuristic circuit is on its way to being completely portable—with an internal power supply and a wireless transmitter. In all likelihood, the combination of wireless monitoring of internal organs with flexible, form-fitting technology will soon give patients and doctors instantaneous information about a wide range of chronic conditions that have long been difficult to manage. *—K.H.*

NEUROSCIENCE

BLOOD TESTS FOR MENTAL ILLNESS

Levels of particular proteins could offer a new way to diagnose schizophrenia and depression

Sabine Bahn wants to change the way psychiatrists diagnose severe mental disorders. She has spent the past 15 years probing the blood and brains of patients with schizophrenia and bipolar disorder (in which someone's mood vacillates between mania and depression), searching for proteins that signal a person's likelihood of developing these conditions. The molecules, known as biomarkers, promise a far more objective way to identify mental illnesses than the usual approach—making diagnoses based largely on patients' self-reported behaviors.

Although biomarkers have improved diagnostic methods for many illnesses—among them diabetes and heart disease—they have not, so far, proved as helpful for psychiatric diseases. Still, Bahn, who heads a laboratory at the University of Cambridge, and a few other neuroscientists are convinced that biomarkers will soon become an indispensable component of psychiatry's tool set. Two blood tests—one of which is based on Bahn's research—are already commercially available.

In 1997 Bahn began scouring brain tissue that had been preserved from schizophrenic men and women who had died. She found that, compared with brain tissue from healthy people, the specimens she examined had unusually high or low levels of at least 50 proteins. Nineteen of the proteins were involved in the operation of mitochondria—the tiny, energy-producing organelles in cells. Bahn also found evidence that the neurons of schizophrenics could not use glucose efficiently, relying on a different molecule—lactate—as an alternative source of energy.

By 2006 Bahn found similar biochemical differences in the cerebrospinal fluid and blood of living people with schizophrenia. In two of her most recent investigations, she distinguished schizophrenic patients from healthy patients with around 80 percent accuracy by examining levels of 51 proteins in the blood. This group of biomarkers includes the stress hormone cortisol and a protein known as brain-derived neurotrophic factor (BDNF) that encourages the growth of new neurons, as well as the establishment of new connections between existing neurons.

Based on Bahn's research, the Austin, Tex.–based laboratory Myriad RBM has developed a $2,500 blood test for schizophrenia called VeriPsych, which measures the amounts of the various proteins that she has identified. Although the test has not received approval from the U.S. Food and Drug Administration, psychiatrists are allowed to use it as part of their practice. (Some tests restricted to a single lab do not have to be FDA-approved as long as they meet rigorous standards for use in people.)

Similarly, San Diego–based Ridge Diagnostics has developed a biomarker test for depression that the company provides through a North Carolina lab for $745. MDDScore, as the test is called (MDD stands for "major depressive disorder"), searches the blood for 10 biomarkers, including BDNF and cortisol.

Researchers have not yet validated these blood tests in clinical trials—except for small studies funded by the companies themselves. Still, a few psychiatrists have found the tools helpful in distinguishing schizophrenia from a temporary drug-induced psychosis or in helping depressed patients accept the reality of their condition and the need for treatment. *—F.J.*

MORE TO EXPLORE

Personalized Medicine: www.genome.gov/13514107
Bionic Eye: www.ncbi.nlm.nih.gov/pmc/articles/PMC2801810
Zeroing In on Cancer: http://nano.cancer.gov
Smart Implantable Devices: www.ted.com/talks/eric_topol_the_wireless_future_of_medicine.html
Blood Tests for Mental Illness: www.nap.edu/catalog.php?record_id=11947

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Read an in-depth report on advances in medical technology at ScientificAmerican.com/may2012/med-tech

EVOLUTION

Triumph of the

The long-necked dinosaurs known as sauropods, once seen as icons of extinction, thrived for millions of years all around the world

By Kristina A. Curry Rogers and Michael D. D'Emic

Titans

APATOSAURUS, formerly known as *Brontosaurus,* exhibits the classic sauropod silhouette: a lengthy spinal column, tapered on both ends, topped with a small-brained skull and balanced on four pillarlike legs. Over the course of their long reign, sauropods evolved various body sizes and different teeth and snout shapes, but their basic architecture stayed the same.

Photograph by Christopher Griffith

Kristina A. Curry Rogers is a vertebrate paleontologist at Macalester College. Her research centers on the evolution and paleobiology of sauropods. She has traveled the world—from Argentina to Zimbabwe—in search of dinosaur fossils.

Michael D. D'Emic is a vertebrate paleontologist at Georgia Southern University. His fieldwork focuses on early Cretaceous sauropods from Montana and Wyoming. He is particularly interested in a group of sauropods known as the titanosaurs.

Ever since fossils of the behemoth, long-necked dinosaurs known as sauropods surfaced in England nearly 170 years ago, they have awed and confused scientists. Even when the great English anatomist Sir Richard Owen recognized in 1842 that dinosaurs constituted a group of their own, apart from reptiles, he excluded the gigantic bones later classified as sauropods. Instead he interpreted them as belonging to a type of aquatic crocodile, which he had named *Cetiosaurus,* or "whale lizard," for the enormous size of its bones. Nearly 30 years later, in 1871, University of Oxford geologist John Phillips would report the discovery of a *Cetiosaurus* skeleton sufficiently complete to reveal that, far from being an aquatic crocodile, the animal spent at least some of its time on land.

Phillips's assessment caused considerable consternation among paleontologists for decades—they just could not conceive how such a massive animal could support its weight on land. Because sauropods were perceived as animals without a place, unsuited for land or sea, they came to be seen as unwieldy, overgrown, archaic herbivores fated for rapid extinction or, at least, marginalization by more "advanced" dinosaurs. As recently as 1991, scientists argued that sauropods were far from the apex of dinosaur success and only flourished in the absence of more specialized plant-eating dinosaurs. In this view, these giants of the Jurassic period, between about 200 million and 145 million years ago, gave way to bigger-brained, better-adapted herbivores in the Cretaceous, between some 145 million and 65.5 million years ago, such as the duckbilled hadrosaurs and horned ceratopsians, which outcompeted the sauropods and pushed them to the fringe.

Relegated to the Southern Hemisphere, so the story goes, only a handful of sauropod stragglers held out to the end of the Cretaceous, when an asteroid impact brought the dinosaur era to a close.

This view of maladapted sauropods plodding along to obscurity was itself destined for extinction. Recent discoveries of sauropods from locales around the world—more than 60 new species in the past 10 years alone—have revealed an extraordinarily resilient group that flourished for millions of years at the observed limits of terrestrial body size. Thanks to such finds and new analytical tools for evaluating them, scientists have begun to answer key questions about how sauropods reproduced, how they grew, what they ate and how they adapted to dramatic environmental change. These revelations have changed almost everything that we thought we knew about this iconic group.

BEYOND THE BIG FOUR

LIKE MOST PEOPLE, the two of us first encountered the long-necked giants of the dinosaur world amid the cacophony of kid-filled natural history museums. Towering above the din of excited

IN BRIEF

Paleontologists traditionally viewed the long-necked, small-brained giant dinosaurs referred to as sauropods as doomed creatures unfit for life on land or in the water.

Recent discoveries have upended that scenario, revealing that sauropods prospered for nearly 150 million years.

The secrets of their success seem to have been their mix of mammal-like and reptilelike traits, combined with an ability to adapt to a changing world.

PHOTOGRAPHED ON LOCATION AT CARNEGIE MUSEUM OF NATURAL HISTORY (*preceding pages*) field-trippers stood the stately sauropod: longer than two school buses, its neck and skull stretched far above the crowds and the other dinosaurs. Even in dust-covered silence, the bones inspired awe. Most of the classic sauropods—such as *Diplodocus, Camarasaurus* and *Apatosaurus*—made their debut in the late 1800s, and by the turn of the century every major natural history museum had to have one. Jurassic sauropod bones flowed into museums in such great numbers that it is still possible to find shelves of these fossils in the bowels of their collections, encased in plaster field jackets, waiting to be opened and studied.

But those classic sauropods represented only a small fraction of the diversity of this group. The story of how sauropods originated and how they evolved into so many forms over their 150-million-year evolutionary history begins even before their appearance—about 210 million years ago in the late Triassic, a time when the world witnessed an extinction event of other reptile groups that cleared the path for dinosaurs and their subsequent dominance of terrestrial ecosystems.

The oldest known dinosaurs in the fossil record are small-bodied, bipedal animals whose remains were found in roughly 230-million-year-old sediments in the Southern Hemisphere; these animals would eventually evolve into the more familiar sauropods and theropods (such as *Tyrannosaurus rex*). Paleontologists have found characteristic trackways of true sauropods—with their quadrupedal posture and elephantine feet—dating to around 225 million years ago in North America and in Argentina. The oldest hints of their massive skeletons are just a little younger, represented by creatures such as *Isanosaurus* from Thailand, *Gongxianosaurus* from China and *Vulcanodon* from Zimbabwe. These early species already bear the signature sauropod stamps: they were walking backbones (many sauropod species have more than 100 vertebrae), with long, tapering necks and tails, tiny skulls, and pillarlike limbs made for bearing serious weight. That basic architectural plan would persist in sauropods for their entire evolutionary duration, making them among the most recognizable of any dinosaur group.

Even in the twilight of dinosaur times, sauropods were diverse and still living large.

Sauropods did not stagnate, however. Their body plan got more elaborate as time played on, with plate tectonics helping to drive the global diversification of their lineages. Sauropod diversity waxed and waned throughout the evolutionary history of the group—right up to the end of the dinosaur era. These recurrent spikes in diversity contradict the long-standing view that sauropods hit their short-lived prime in the Jurassic and limped along to their nadir in the Cretaceous. Instead we see important sauropod groups, such as the stocky titanosaurs and the shovel-faced rebbachisaurids, flourishing long after this presumed Jurassic heyday. Even in the twilight of dinosaur times during the Late Cretaceous, sauropods were diverse and still living large.

SIZING UP SAUROPODS

New discoveries have shown that sauropods were successful in terms of geographic range, diversity and the longevity of lineages. But what exactly were their strategies for getting by in the world? The answer seems to be that they made use of a special mix of reptilelike and mammal-like characteristics, which merged to create truly unique organisms. Although Sir Owen was wrong in thinking that sauropods were lizards, in this respect his "whale lizard" name turned out to be fairly apt after all.

In their reproductive habits, sauropods, like all dinosaurs and most reptiles, hatched from eggs. The first concrete evidence for sauropod reproductive biology came from roughly 80-million-year-old deposits at Auca Mahuevo in Argentina, where in 1997 Luis Chiappe of the Natural History Museum of Los Angeles County and his colleagues found a sauropod nesting ground containing thousands of eggs. Inside some of the eggs, the researchers found the first known embryos of sauropods, some of which preserve fossilized skin and egg membranes.

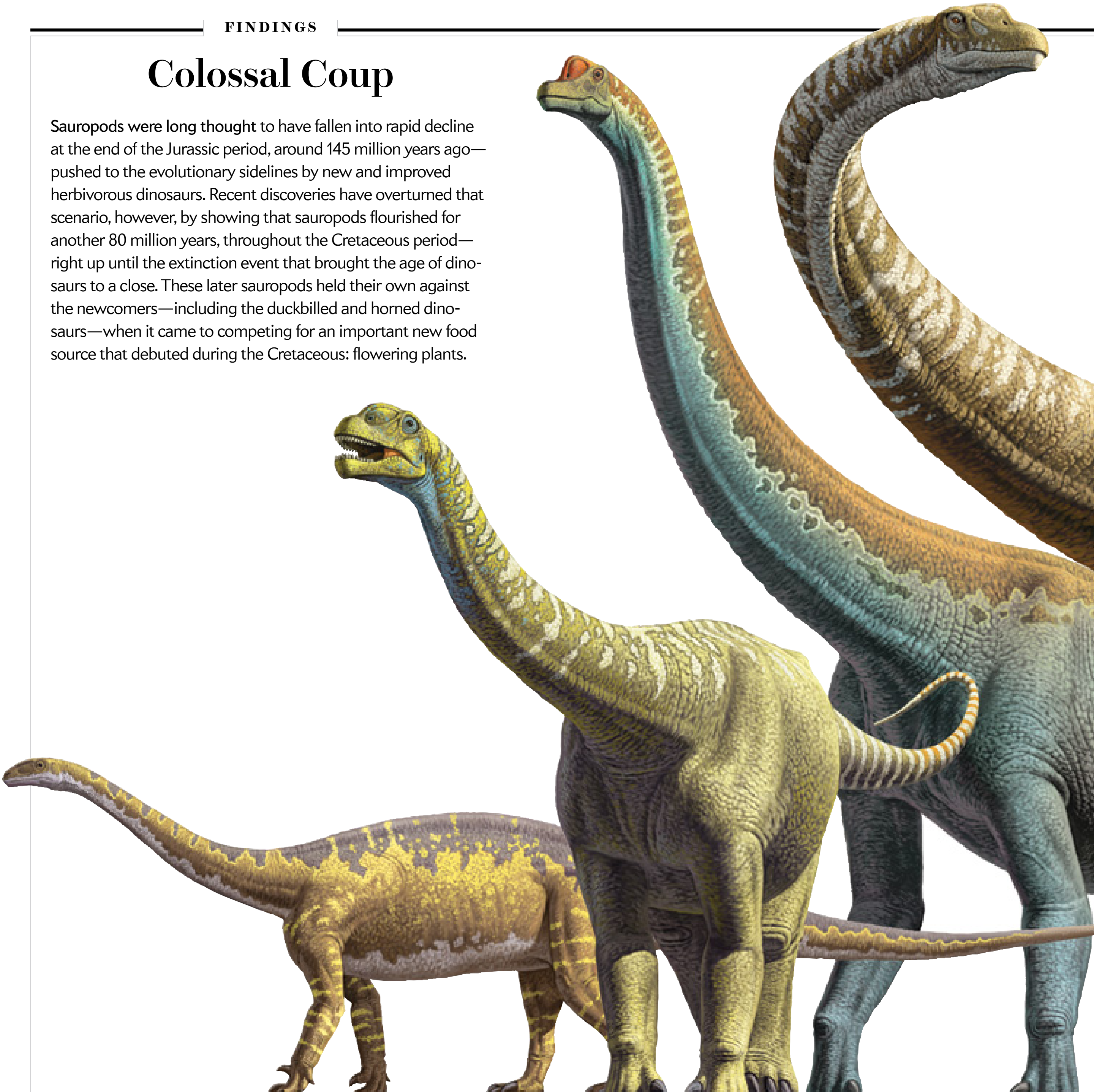
These nesting traces provide clear evidence that titanosaur sauropods laid 20 to 40 spherical eggs per clutch in excavated depressions. The eggs are relatively small, averaging 13 to 15 centimeters in diameter, about the size of a grapefruit. The abundance of nests in the same layers at Auca Mahuevo suggests that the titanosaurs there associated in large groups and nested at the same area at least six times. Still, no convincing evidence exists that they sat on the eggs or cared for the young once they hatched. In fact, the proximity of the nesting structures to one another suggests that these titanosaurs were hands-off parents. Unlike other large-bodied vertebrates, such as elephants and whales, in which parents invest heavily in raising a single offspring, sauropods apparently stuck with the typical reptilian pattern of producing many offspring that were then left to fend for themselves.

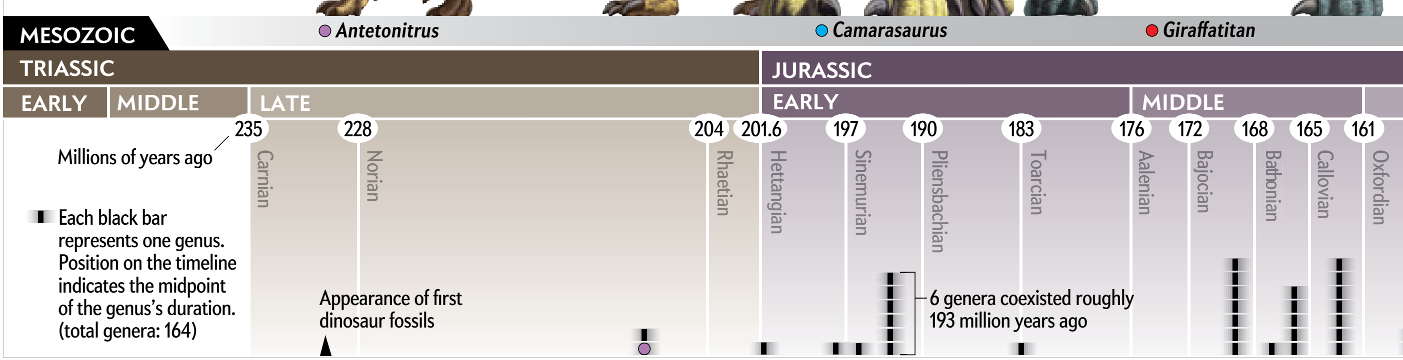
Although sauropod parental investment hewed to the reptilian norm, the growth rates of these animals did not. Sauropods had the furthest to grow from newborn to adult of any animal ever to live. Baby sauropods were less than half a meter long and weighed less than 10 kilograms. As adults, the largest sauropods attained body lengths of 30 meters and body masses between 25,000 and 40,000 kilograms or more. For comparison, the average baby African elephant weighs around 120 kilograms at birth and reaches an adult weight of 2,268 to 6,350 kilograms. Most early dinosaur researchers simply extrapolated reptilian growth rates to estimate sauropod growth history. In this model, even smaller sauropods would have taken until age 60 to experience their first growth plateau and more than a century to reach adult size. That would mean waiting until age 60 to reproduce—risky business for any animal that stays relatively small and predator-prone for a big part of life.

A different perspective on sauropod development began to emerge in the 1960s, when Armand de Ricqlès of the College of France in Paris began to study the internal microstructure, or histology, of bone for insights into the life history of dinosaurs and other extinct animals. The patterns of bone mineral, the density and architecture of the cavities left behind by blood vessels, and the degree of bone remodeling are all preserved in fossil bones. These features indicate that sauropod growth rates soared through most of life and that they were generally faster than the growth rates of reptiles and on par with those of living large-bodied mammals, many of which mature within decades. Therefore,

Colossal Coup

Sauropods were long thought to have fallen into rapid decline at the end of the Jurassic period, around 145 million years ago—pushed to the evolutionary sidelines by new and improved herbivorous dinosaurs. Recent discoveries have overturned that scenario, however, by showing that sauropods flourished for another 80 million years, throughout the Cretaceous period—right up until the extinction event that brought the age of dinosaurs to a close. These later sauropods held their own against the newcomers—including the duckbilled and horned dinosaurs—when it came to competing for an important new food source that debuted during the Cretaceous: flowering plants.



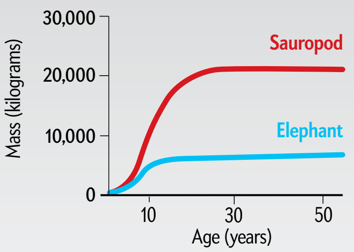


Illustrations by Raúl Martin, Graphics by Jen Christiansen

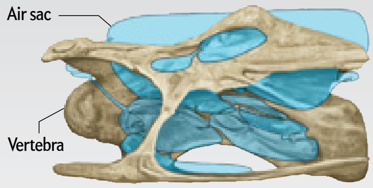
Survival Tricks

Sauropods benefited from a host of adaptations to living large on land, thus allowing them to reach sizes unequaled by any terrestrial animal since.

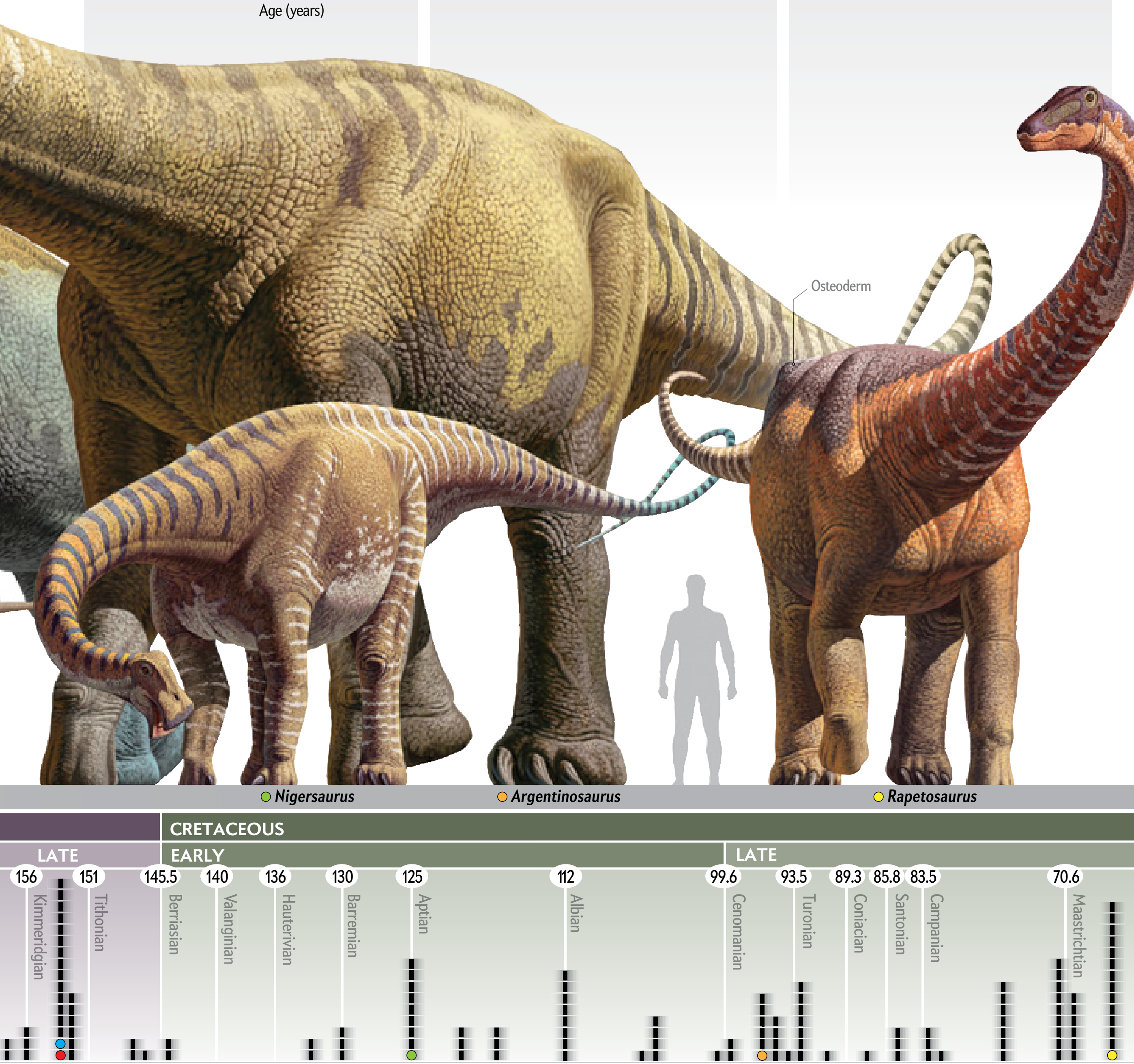
Unlike most reptiles, sauropods grew fast—akin to modern terrestrial giants, such as elephants—and would have reached adult size in a few decades.



Hollow vertebrae would have lightened sauropod bodies and may have permitted the expansion of air sacs from the lungs that could have allowed them to take in more oxygen with each breath.



Bony plates called osteoderms, which were embedded in the skin of some sauropods, may have served as mineral reserves in hard times. As an animal aged, its osteoderms grew hollow from donating their calcium to the blood.



SOURCES: DANIELA SCHWARZ-WINGS *Museum of Natural History, Berlin (vertebra detail)*; KRISTINA A. CURRY ROGERS AND MICHAEL D. D'EMIC *(growth curves)*; GEOLOGICAL SOCIETY OF AMERICA *(geologic timeline)*

SNACK-SIZE SAUROPODS: Sauropods may have been untouchable as adults, but as babies they were highly susceptible to predators large and small. In 2010 Jeffrey Wilson of the University of Michigan and his colleagues described a clutch of sauropod eggs from India that includes a fossilized 12-foot-long snake coiled around and crushing one of them, alongside a tiny sauropod hatchling—as shown in the artist's reconstruction above. Several such examples from their field area of snakes associated with dinosaur eggs support the idea that these snakes frequented sauropod nesting grounds and feasted on eggs and hatchlings.

COURTESY OF TYLER KEILLOR

sauropods did not have to live for centuries to become giants.

With such rapid growth rates and enormous adult body sizes, sauropods must have had prodigious appetites. Indeed, one of the most perplexing mysteries of sauropod biology is how these giants gathered enough plant matter to survive, much less thrive, for so long. Traditional studies of sauropod feeding focused on tooth shape, microscopic wear marks, jaw muscle reconstructions, and analyses of the biomechanics involved in opening and closing the jaw. This research has revealed that different sauropods employed distinctive feeding methods—some bit off tough vegetation, whereas others cropped or clipped softer plants.

Researchers generally agree that sauropods did not do a lot of chewing and thus most likely required some "postmouth" processing to break down plant food into usable energy. The most commonly cited solution to this need for extra processing is the use of gastroliths—or stomach stones, as they are known. Polished stones often turn up in sauropod-bearing rock formations in western North America, and scientists have long hypothesized that these stones are analogous to the gastroliths that some modern vertebrates, such as certain birds, ingest to help grind up food and aid in digestion. In 2007, however, Oliver Wings of the Museum of Natural History in Berlin and Martin Sander of the University of Bonn in Germany took the notion of sauropod gastroliths to task in an experimental analysis of how gizzard stones in living birds are processed and degraded. Their study showed that purported sauropod gastroliths lack the surface texture expected when compared with the true gastroliths of birds. Moreover, evidence of gastroliths discovered inside sauropod body cavities was scarce and equivocal. They thus concluded that, like modern big herbivorous animals such as rhinos, sauropods relied on microbial fermentation in their incredibly elongated digestive systems, not gastroliths, to extract energy from the plants they ate.

Additional insights into sauropod feeding strategies have come from studies of their most distinctive trait: that trademark long neck. Conventional wisdom held that the animals used their necks to dine in the treetops, reaching leaves unattainable by other dinosaurs. New research has challenged this view. John Whitlock of the University of British Columbia reconstructed feeding strategies among diplodocoids, a group of sauropods that includes the familiar *Apatosaurus* and *Diplodocus* that persisted from the Late Jurassic to the Late Cretaceous. Variation in snout shape and microscopic wear patterns on teeth indicate that some sauropods specialized in particular kinds of plants and others were generalists; whereas some grazed on ground-height plants, others fed from the trees. Different research groups have drawn similar conclusions from analyses of sauropod neck postures, which show that sauropod feeding was additionally constrained by vertebral flexibility: sauropods varied in their ability to crane their necks to reach plants up high and down low. This diversity of dining habits helps to explain how so many giants shared the same ecosystems.

Sauropod dietary adaptations flourished in the Cretaceous, concurrent with the rise of flowering plants. An old-school hypothesis held that other dinosaurian vegetarians better suited to dining on these new plants pushed sauropods to the evolutionary sidelines in the Cretaceous. In this view, sauropods, with their weak teeth, small heads and giant bodies, were no match for the more efficient duckbills and horned dinosaurs, which possessed conveyor belts of teeth packed together to form formidable dental batteries that acted as one giant, ever growing powerful tooth.

What we now know is that the Cretaceous was actually the most diverse interval of sauropod evolution and arguably the most interesting. Far from being outcompeted by newcomers, sauropods diversified in form and function, evolving novel means of exploiting a wide variety of plants. Take, for example, *Nigersaurus:* a 115-million-year-old species discovered in Niger in the mid-1990s by Paul Sereno of the University of Chicago and his colleagues. The creature evolved broad dental batteries with extremely fast tooth replacement rates (one new tooth in each position every month, which is up to twice as fast as those of duckbills and horned dinosaurs), keeping teeth sharp for efficient clipping of vegetation. The orientation of the semicircular canals of the inner ear—the organs of balance—in *Nigersaurus* suggests that this animal usually held its head with its muzzle pointing directly downward, rotated 70 degrees from the usual horizontal pose inferred for other sauropods. This position suggests that it specialized in feeding on plants near the ground.

As the Cretaceous progressed and flowering plants diversified, sauropods found themselves with more options on the table. Microscopic analysis of fossilized feces, or coprolites, from titanosaurs has revealed silicified plant tissues called phytoliths that document at least five different types of grass in addition to such flowering plants as magnolias, conifers and palms. This discovery, reported by Vandana Prasad of the Birbal Sahni Institute of Paleobotany in India and her colleagues in 2005, pushed the origin and diversification of modern grasses back by some 30 million years and supports the notion that some sauropods fed fairly indiscriminately. As is true for any respectable fast-growing vertebrate herbivore, it paid for sauropods to not be picky. Far from being pushed out of these emergent ecosystems, they seem to have taken full advantage of the new resources, eating everything from the tops of trees to the forage at their feet.

Enhanced oxygen intake may have further fueled sauropod growth. In living birds, air sacs connected to outpocketings of the lungs invade their hollowed-out vertebrae, allowing the birds to suck more oxygen out of each breath than mammals can. Air sacs in birds allow for a unidirectional airflow through the lungs, which increases the oxygen content extracted from each breath. (In mammals, airflow is bidirectional: each new breath mixes in our lungs with old air, resulting in a relatively inefficient method of oxygen extraction.) Sauropod vertebrae resemble those of modern birds in having nearly identical internal cavities and a complex pattern of external hollows bounded by struts. The greatest hollowness, or pneumaticity, is found in neck and trunk vertebrae, but in some sauropod species it can extend as far back as the hips and tail. The primary effect of pneumatization is overall reduction in the weight of the vertebral column, and estimates indicate that it may have significantly reduced sauropod body mass. For example, the North American colossus *Sauroposeidon* had a neck that was more than 75 percent air. It is also possible that, as in birds, the pneumatized vertebrae of sauropods housed an extensive air sac system with flow-through ventilation of the lungs that aided respiration and would have allowed them to maintain stable, high metabolic rates and increased activity levels consistent with their elevated growth rate and massive adult body size.

WHEN THE GOING GOT TOUGH

BEING BIG had a real advantage for sauropods, as it does for modern behemoths. Even before they were halfway grown, many sauropod species exceeded the size of adult elephants, which have essentially no predators (apart from humans). Once they reached adult size, they were probably fairly immune to serious predators, such as *Allosaurus*. Large body size also left sauropods extra vulnerable in cases of food and water shortage. Yet some may have evolved solutions to even that problem: a handful of titanosaur species bore bizarre bony plates in their skin called osteoderms. A number of modern animals have osteoderms—they make up the armorlike covering of crocodilians, lizards and armadillos, and they formed the distinctive bony plates and spikes in dinosaurs such as *Stegosaurus*. Where on the sauropod body osteoderms resided has been impossible to determine, however, making it hard for scientists to discern their function.

New findings may resolve this question. We recently described two osteoderms that were found in Madagascar alongside one juvenile skeleton and one adult skeleton of a titanosaur called *Rapetosaurus*. At 57 centimeters long and more than 27 centimeters thick, with a volume of nearly 10 liters, the adult specimen is the most massive osteoderm ever discovered from any backboned animal. CT scans and drill cores indicate that the osteoderms of *Rapetosaurus* hollowed out during the course of the animal's life, and at very large sizes about five liters' worth of internal bone was replaced, probably with soft tissue. Instead of the pavementlike covering of osteoderms found in living animals, *Rapetosaurus* (and probably some other titanosaurs) had only a few large plates.

These features of the *Rapetosaurus* osteoderms helped us rule out several competing ideas about the function of osteoderms in titanosaurs. Such internally hollow elements would offer little in the way of protection because they would shatter under the force of a predator's jaws. Similarly, the low surface area to volume ratio of the elements and their sparse distribution in the skin would have rendered them useless for thermoregulation. We argue that titanosaur osteoderms instead served as an invaluable mineral reserve that may have helped sustain growth rates and egg-laying ability even through the harshest times, just as they do in some modern animals. In all living vertebrates, including humans, bone mineral is sacrificed to help maintain blood calcium levels. This remodeling often increases seasonally, when resources are rare, during egg laying and with increasing age—which in humans leads to osteoporosis. Osteoderms have rich blood supplies that serve as the perfect conduits for the cells that do the remodeling and for the mineral resources that are unlocked from deep inside bones. This idea makes a lot of sense for a massive sauropod in Late Cretaceous Madagascar. Back then, the island was a harsh place to live—regular, severe droughts forced meat-eating dinosaurs such as *Majungasaurus* to cannibalize members of its own species and brought about the demise of innumerable animals, from frogs and birds to sauropods. Osteoderms may have helped sauropods in Madagascar and elsewhere survive environmental perturbations, including frequent, intense droughts.

Sauropods seem to test the laws of biological possibility in how fast they grew and how large they became. These breaches could have painted them into an evolutionary corner, yet our growing knowledge of the fossil record suggests the opposite. Indeed, they went extinct, but before that inescapable disaster struck, sauropods had a spectacular 150-million-year run as one of the most remarkable extravagances that evolution has ever invented. SA

MORE TO EXPLORE

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SCIENTIFIC AMERICAN ONLINE
For an interactive sauropod graphic, see **ScientificAmerican.com/may2012/sauropods**

Jerry Adler was a senior editor at *Newsweek* from 1979 until 2008. He has written on topics ranging from profiles of Stephen Hawking and Sally K. Ride to a cover story on America's infatuation with self-esteem.

NEUROSCIENCE

ERASING PAINFUL MEMORIES

The caustic imprint of a traumatic memory may fade or vanish with new drug and behavioral therapies

By Jerry Adler

THE RAT IS ON A CAROUSEL WITH CLEAR PLASTIC SIDES, rotating slowly in a small room. As it looks out through the plastic, it sees markings on the walls of the room from which it can determine its position. At a certain location it receives a foot shock—or, in experimenters' jargon, a negative reinforcement. When that happens, the rat turns sharply around and walks tirelessly in the opposite direction, so it never reaches that same place in the room again. It will do this to the point of exhaustion.

Question: How do you get the rat to stop walking? Note that just turning off the shock will not suffice, because the rat will not allow itself to enter the danger zone. The rat needs an intervention that helps it forget its fear or that overrides its response with a competing signal of safety.

So much for the rat. Now think of someone who has been wounded in combat and suffers from the vague but real cluster of symptoms called post-traumatic stress disorder (PTSD). He, too, associates specific contexts or stimuli—open spaces, crowds, sudden loud noises—with something painful. He avoids those circumstances when he can. He is in the same bind as the rat on the turntable: unable to discover for himself that certain situations are now safe. How do we get him to stop running?

The rat on the carousel and the veteran on a crowded street are both prisoners of memory, of the extraordinary power of pain to forge an indelible impression on the brain: be it mammalian, reptile or even invertebrate. As some researchers labor to solve the mystery of memory loss in dementia, others are attacking the mirror-image problem of how to help patients escape the painful memories that dominate their daily life—and not just those with PTSD. An emerging new paradigm views such diverse conditions as phobias, obsessive-compulsive disorder, and even addiction and intractable pain as disorders of

FREDRIK BRODEN

learning and memory or, more pointedly, forgetting.

Some people never forget the time a spider fell into their glass of milk. Others cannot break the association of certain places or situations with getting high. Now researchers are finding that remembering is not just a process of passively storing impressions. It is a continuous, dynamic activity on the cellular level and an ongoing psychological process open to manipulation with drugs and cognitive therapy. This is wonderful news for combat veterans and victims of assaults and accidents. What it means for future generations of historians and personal-injury lawyers remains to be seen.

For the rat on the carousel, you can imagine different approaches to extinguishing its fear. You could let it walk to exhaustion and learn for itself that the shock has been turned off—a process psychologists call extinction. Or you could try tinkering directly with the rat's brain—specifically, the hippocampus, where place memories are formed and stored. Six years ago neuroscientist Todd Sacktor of S.U.N.Y. Downstate Medical Center in Brooklyn, building on work with his former colleague André Fenton, did just that. He injected a compound called ZIP into the hippocampus of a rat that had been trained on the carousel and, after two hours, tested it again and found the fear had been erased. Do that in a combat veteran disabled by PTSD, and you are on the way to a Nobel Prize or a billion-dollar drug bonanza.

To understand Sacktor's experiment in forgetting involves some exploration into memory—and how the learning processes that underlie recollection can ultimately be undone. Neuroscientists who specialize in memory often start by considering long-term potentiation (LTP), the process by which two or more neurons that fire simultaneously, or in close sequence, develop a synchronous bond that makes them likely to fire together in the future. Basically the neuron that encodes the experience of hearing a sudden loud bang can become associated with the neurons that cause you to look for cover and drop to the ground.

The complex biochemistry of LTP involves the proliferation of glutamate receptors on the receiving, or postsynaptic, cell to amplify the electrochemical signal that crosses the tiny gap between one neuron and another. But, as Sacktor explains, these receptors are unstable; they are continually forming, disappearing and re-forming. A memory's persistence implies the existence of an active biochemical process that keeps a fixed complement of receptors in place.

The agent involved in memory preservation was long assumed to be a protein because drugs that block protein synthesis systemically can prevent learning and memory formation in animals. Sacktor's laboratory zeroed in on an obscure protein kinase—an enzyme that activates other proteins by attaching a phosphate group to them—known as PKMzeta. It is PKMzeta, Sacktor says, that is responsible for sustaining memories; without it, long-term potentiation fails, and the memory evaporates. PKMzeta has a specific antagonist, called ZIP, which was what Sacktor injected into the rat's hippocampus to make it forget its aversion training on the carousel. Merely by blocking the continuing action of PKMzeta, ZIP acts on memory as if it were reformatting a hard disk.

For that very reason, ZIP is not likely to be tried on humans anytime soon as a drug for blotting out bad memories. If it could be chemically modified to prevent it from entering the brain, confining its activity solely to the spinal cord, it might one day turn up as a treatment to erase the hypersensitized reaction of the chronic pain sufferer to a poke or prod, a reaction that itself is a form of memory. For obliterating recall of traumatic events, the need is for a drug with the power of ZIP but enough specificity to target individual memories.

At first glance, the problem seems insoluble because there appears to be no biochemical distinction between good and bad memories that ZIP could exploit. A few research endeavors point toward ways around this issue. None are effective enough to completely blot out a specific unwanted memory, but they may still blunt some of the anguish associated with the painful recall of a disastrous event.

The hypothesized weak spot in the development of PTSD is consolidation, the process of moving significant memories from short- to long-term storage. The line between short and long term is difficult to quantify but simple to illustrate: you probably remember what you ate for dinner last night but not a year ago—unless it was your wedding reception or a meal that sent you to the emergency room. Long-term memories tend to be formed around emotionally significant or fearful events—or anything that releases the neurotransmitter norepinephrine, which promotes protein synthesis in the amygdala. As one famous experiment showed, even sticking a hand in a bucket of ice water will work.

By the same token, you ought to be able to interfere with long-term memory formation by lowering levels of norepinephrine. Several candidate drugs do just that, of which the best known is the beta blocker propranolol, widely used to treat hypertension and stage fright. (It is a fact of life for biomedical researchers that unless they work for a drug company with hundreds of millions of dollars to spend on human trials, they are more or less forced to experiment with drugs that are already approved for human use in another condition.) The window in which consolidation takes place is still being investigated, but it appears to be on the order of a few hours. In the early 2000s Roger Pitman, a neuroscientist at Harvard Medical School, got the idea of giving people propranolol right after a traumatic event—in his case, after an auto accident or an assault because he was working with civilians—to see whether blocking norepinephrine could in effect inoculate them against post-traumatic stress.

Note that Pitman's intent was not to erase the memory of the trauma itself—

IN BRIEF

Toxic memories are the basis of pathologies from phobias to pain. Legions of neuroscientists have tried to marshal our understanding of how memories form in the brain to try to reverse this process in patients who need to escape the legacy of psychological or physical trauma.

ZIP, an eponymous biochemical, wipes a rat's memory but is incapable of selecting only "bad" memories for removal.

Turning down the level of pain associated with anticipated trauma or a just experienced ordeal may come about from administration of drugs that decrease the levels of stress-related norepinephrine.

A rewrite of personal history may represent yet another strategy. When old memories are recalled, drugs or behavioral therapies might alter the tainted emotional coloration surrounding them.

the episodic, autobiographical recall of the event—only the emotional valence associated with it. In theory, doing so runs the risk of compromising the psychological integrity of victims, a concern that would certainly arise if it were possible to alter the contents and not just the emotional tone of memories. Long after American society made peace with the idea of using drugs to alter consciousness and mood, memory, the sacred vessel of selfhood, remains off-limits to manipulation in the view of many. "I've had to debate the bioethicists every year on this," says one of the pioneers of modern memory research, James McGaugh of the University of California, Irvine. "They make their living worrying about this—whether it's a good idea to diminish traumatic memories, notwithstanding that people all the time tell [trauma victims], 'There, there, you'll get over it.' That's a good thing. Giving them a drug isn't. Now why is that?"

McGaugh himself, in a classic experiment with his U.C. Irvine colleague Larry Cahill in the 1990s, showed that propranolol could affect, if not the accuracy, at least the specificity of episodic memories. These experiments were typically done with illustrated stories. McGaugh and Cahill presented subjects with either of two different variations on a story: one about a boy hit by a car and needing emergency surgery, the other about an emotionally neutral account of a visit to a hospital. The first group, as expected, remembered the story in much more detail. But when the experiment was done again, with subjects given propranolol the difference disappeared—the emotionally arousing story was remembered just as well as the neutral one.

One can envision prosecutors or personal-injury lawyers being made nervous by the prospect of anything that affects the recall of crime or accident victims. Even with factual memories unimpaired, a few tears on the witness stand can be worth more than their weight in gold when a jury is awarding damages. But it is also worth bearing in mind that the comparison is to a hypernormal state of recall induced by a rush of norepinephrine. All propranolol can do, though, is bring emotionally charged memories into line with recollections of neutral events. And from the victim's point of view, that might be just what the doctor, if not the lawyer, ordered.

Pitman's first report on using propranolol on trauma victims, published in 2002, showed some encouraging results, leading to exuberant predictions that before long patients arriving at an emergency room or a military field hospital would be evaluated for potential PTSD, just as they are x-rayed for broken bones, and treated accordingly. But a follow-up study published in 2011 failed to support the hypothesis. It also demonstrated just how hard this research is in the real world. Over a period of 44 months only 173 of 2,014 patients screened met the study criteria, the rest having been rejected for reasons of age, preexisting medical condition or insufficient trauma. Among other difficulties, federal law now forbids researchers from approaching patients directly; permission has to be obtained first by a clinical caregiver, typically an emergency medical specialist with more urgent things on his or her mind. "We just didn't have much luck in getting to them" soon enough, Pitman says. "I wouldn't do another propranolol study unless I could get them the drug much sooner, and I don't see that happening. On the other hand, if people call me and say, 'I've just been in an accident. Should I take propranolol?' my answer is, 'I can't support it based on the data, but I still think it has potential.'" Drugs, though, may not be the only answer.

Take the subject sitting in an office at the Emory University School of Medicine. In his mind, he is years back in time and thousands of miles away, at the wheel of a Humvee in Iraq. The script playing out on the virtual-reality goggles he wears is drawn from his memory and is being fed back to him in real time by a therapist at a keyboard. Following his account, she plants an imaginary sniper on an overpass, detonates a land mine on the road and sends shadowy figures running down an alleyway. The chair shakes with each explosion. Now the subject is breathing hard, looking urgently to the left and right, wrenching an imaginary steering wheel. He breaks out in sweat and throws an arm up to protect his face.

REPLACEMENT REALITY: An army sergeant who treats PTSD tries out an experimental virtual-reality system intended to quell uncontrollable postcombat fears.

TED S. WARREN *AP Photo*

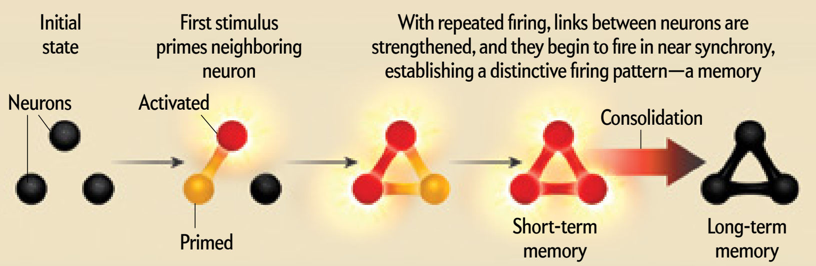
As soon as Russian psychologist Ivan Pavlov discovered the mechanisms of classical conditioning, it was natural to ask about the opposing phenomenon of extinction: If you rang the bell and did not feed the dog, how long would it be before he stopped salivating? Not very long, it turned out, leading to a question that is still worth asking: Why does PTSD not self-extinguish in the same way? The world, after all, is full of sudden loud noises that do not signify a mortar attack, and yet some people never seem to unlearn the responses they learned in Afghanistan or, for that matter, Vietnam. One way to think about this is that in PTSD, anxiety and distress become, in effect, their own negative reinforcement; reliving the original trauma with each succeeding reminder is

MEMORY BLOTTER

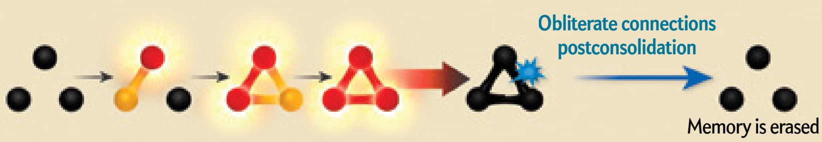
Learning to Forget

Once formed, recollections of trauma may seem indelible. But researchers now believe they are more like files on a hard drive that can be altered, overwritten or even erased. Ridding the brain of toxic memories induced by traumatic life events requires tweaking individual neurons, each of which connects to thousands of others.

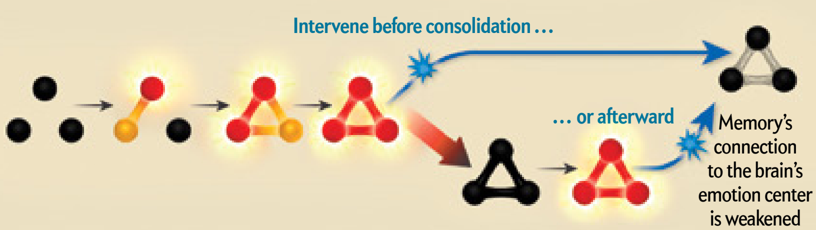
Neuroscientists are now studying biochemical and behavioral measures to assist in forgetting. This line of research starts with the basics of how memories form. A memory arises when a series of neurons fire together in a similar way—a process called consolidation. First one neuron fires in response to a sound, a visual perception or another input, which triggers another to switch on and, later still, other nearby cells. Then, when any neuron is stimulated again, even weakly, other neurons in the network also fire—a physical embodiment of what happens when you recall getting bitten by a neighbor's dog.



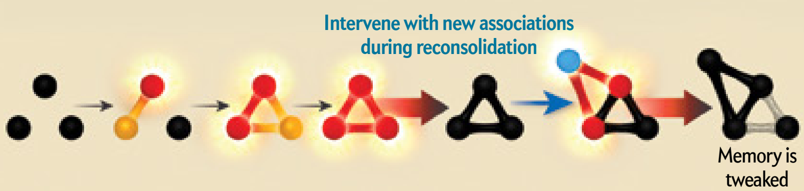
Erase: Blotting out a memory occurs by unlinking interconnected neurons. This involves inactivation of a protein called PKMzeta, which acts as a kind of preservative chemical—ensuring that the connections among brain cells in the network remain intact. A compound known as ZIP serves as a finish remover that unhooks these neural links and abolishes the memory along with it. Researchers have yet to devise a means of targeting specific memories. Simply ingesting a drug like ZIP would cause all recollections to disappear.



Dampen: Instead of wiping the slate clean, other researchers have investigated ways to weaken the connections among neurons in parts of the brain that record or recollect a fearful event. They have tried to do this by administering a drug, such as the beta blocker propranolol, either before an anticipated fright or else during the recall of an incident afterward to allow the drug to dull the painful memory.



Replace: A memory makeover is yet another option. It turns out that when a memory is recalled later, it can be manipulated—through behavioral intervention and perhaps one day with a drug—so that a past incident is brought to mind in a safe setting and then "reconsolidated" in a different emotional light.



painful enough to keep the response intact.

Like the rat on the carousel, human beings are able to escape painful situations—a mixed blessing because it means their responses are not subject to extinction. "We tell them, 'It's like you opened the book to the wrong page and what you see is so frightening that you slam it shut. And so you never learn any differently,'" says Barbara Rothbaum, head of Emory's Trauma and Anxiety Recovery Program. "We want them to read the whole chapter." The veteran in the chair is being exposed, as nearly as virtual reality can approximate it, to the situation in which he was traumatized. Taking advantage of the proximity of the brain's smell center to the amygdala, where emotions are processed, Rothbaum has introduced scents—a bouquet of evocative odors, including gunpowder, Middle Eastern food, sweat and garbage—to the virtual-reality protocol.

Treating PTSD this way is an extension of how Rothbaum has treated phobias in many patients over the years, by exposing them in reassuring contexts to the feared object, usually in small, graduated increments: the word "snake," a picture of a snake, a snake in a cage, and so on. (Virtual reality has been enlisted as well: therapists, who once had to search out glass-walled elevators to treat acrophobia, can simulate, at no cost, high balconies or a jungle full of snakes and spiders.) The extinction process reaches deep into the amygdala, where logic does not penetrate, to implant the message: there is nothing to fear.

Still, extinction is more complicated than it appears. Rather than simply erasing a fear memory, it seems to be a process of forming a new memory, one of safety, that competes with the original trauma. "Extinction is a bad term," says Rothbaum's Emory colleague Michael Davis. "It's not like the dinosaurs. If you put the organism under stress or in a new environment, the fear memory can come back, so it clearly hasn't disappeared." That gave the Emory researchers, Davis, Rothbaum and Kerry Ressler, the idea of trying to enhance extinction with a drug that—in a seeming paradox—accelerates memory acquisition. The drug they are using is D-cycloserine, an antibiotic that is used to treat tuberculosis but that is also active in the brain, where it energizes a structure called the NMDA receptor, a type of glutamate receptor. The receptor is a "biochemical coincidence detector," Davis says,

Illustration by Emily Cooper

which is activated when neurons fire simultaneously. It depolarizes the cell membrane on the downstream neuron, admitting calcium and setting in motion the sequence of reactions leading to long-term potentiation, memory and learning.

From the ease with which fear memories are acquired, Davis concludes that a single frightening event must unleash a flood of them in the amygdala. You do not need chemical help to remember an encounter with a lion, about which the adage "once bitten, twice shy" is profoundly appropriate. Extinction, in contrast, seems to have evolved as a slow, almost reluctant process. Survival is enhanced by remembering danger, not by forgetting it. As Davis says, though, if you have a patient with a germ phobia, and the cure is to make him touch a toilet seat, the dropout rate is pretty high. If the typical course requires eight sessions, and you can do it in two by adding D-cycloserine, that is obviously a big improvement. Clinical trials are now under way to assess how using D-cycloserine can help speed extinction in PTSD. Yet, again, overwriting bad memories may not require popping a pill.

SUBJECTS FACE A COMPUTER SCREEN and trail wires from electrode pads on their wrists and fingers. One set will deliver a shock; the other will record skin conductance, a standard measure of fear. The subjects are in three groups, all of which undergo identical conditioning to expect a shock in association with a blue square shown on the screen. The next day the groups all undergo extinction training, viewing the figure repeatedly without receiving a shock, until they no longer show a reaction to it. Two of the groups, however, get something extra first: a single "reminder" trial, either 10 minutes or six hours before the extinction session. In practice, the reminder trial is identical to a single extinction trial: the subject sees the figure and does not receive a shock. Yet it functions very differently in the brain. The kind of conditioned fear induced by a shock often reappears spontaneously after extinction, and a day later, in two of the three groups, it did. But in the group that received the reminder trial 10 minutes before extinction, there was virtually no spontaneous recovery; extinction somehow was much more effective with them. Amazingly, the difference persisted even one full year later.

How can this be? The answer, according to Elizabeth Phelps, at whose New York University lab the study was done, goes back to consolidation theory—the idea that it requires several hours for memories, together with their emotional valence, to be fixed in long-term storage. The implication is that there is a window during which they can be manipulated, which is what Pitman and his collaborators tried to do, unsuccessfully, in the emergency room at Massachusetts General Hospital. A now famous paper from 2000 by Karim Nader, now at McGill University but at the time a fellow in the N.Y.U. lab of memory researcher Joseph E. LeDoux, revived an earlier, out-of-favor hypothesis: that old memories can be changed when they are recalled to consciousness. In this view, the proper metaphor for memory is not a scrapbook or a diary but a hard drive containing files that can be modified each time they are called up. Memories are "labile" for a period after they are recalled—the function of the reminder trial in Phelps's experiment—and then undergo reconsolidation after several hours.

Debate persists about the evolutionary value of this feature, although the most convincing explanation is that it allows for the updating of memories with new information. Being bitten by a lion and being bitten by, say, a mongoose are very different experiences; once the shock of being attacked subsides and the wound heals, there is survival value in being able to think back and distinguish between them. When Nader, LeDoux and Glenn E. Schafe, now at Yale University, showed in 2000 that the same drugs that block consolidation of new memories in rats could erase existing ones during the reconsolidation window, the race was on to find ways to harness the effect in humans.

Unfortunately, the drugs used in rats, which block protein synthesis systemically, are toxic. Hence, researchers have turned to drugs such as propranolol and mytarapone; the latter inhibits cortisol, another stress hormone that is associated with the formation of emotionally charged memories. (Do not try this at home, but alcohol and morphine might work, too.) The results so far have been inconclusive, reflecting the difficulty of isolating one psychological parameter in conscious, self-aware organisms whose preexisting memories and personalities are considerably more varied than those of most lab rats.

Merel Kindt, a researcher at the University of Amsterdam, reported a few years ago that giving propranolol during reconsolidation reduced fear (as measured by the strength of the electrical potential in the muscles controlling eyeblinks) in subjects who had been conditioned to fear a picture of a spider. Pitman thinks "the jury is still out" on propranolol—which is why there was so much excitement in 2010, when Phelps and her colleagues, including lead experimenter Daniela Schiller, published their reconsolidation study. Their work did not rely on drugs for its effect.

The findings, they wrote, "suggest a non-invasive technique that can be used safely and flexibly in humans to prevent the return of fear." Moreover, "this effect is specific to the targeted fear memory, and not others, and persists for at least a year." The response was so positive, in fact, that Phelps feels the need to caution that the work is "still in its infancy. There are hundreds of papers on rats since 2000 and a handful in humans. Ever since the first animal studies, people have been talking as if we cured PTSD. And for a decade, we hadn't been able to show anything in people—in healthy undergraduates, in the lab, let alone with patients in the real world. Now we've done that, but it took seven years. I made people afraid of a blue square on a screen, and I got them to sweat a little less."

Will propranolol be the answer? Or will it be some as yet undiscovered compound that, in Sacktor's dreams, combines the potency of ZIP with the specificity of reconsolidation blocking? LeDoux thinks memory research is "on the cusp of bearing fruit" in the form of treatments for such crippling disorders as PTSD. Others are less certain. But if we weigh the pain this condition has caused so many people, it is hard to dispute Rothbaum's view: "The primary prevention for PTSD," she says, "is not to have any more wars." SA

MORE TO EXPLORE

PKMζ Maintains Spatial, Instrumental, and Classically Conditioned Long-Term Memories. Peter Serrano et al. in *PLoS Biology,* Vol. 6, No. 12, pages 2698–2706; December 23, 2008.

Preventing the Return of Fear in Humans Using Reconsolidation Update Mechanisms. Daniela Schiller et al. in *Nature,* Vol. 463, pages 49–53; January 7, 2010.

SCIENTIFIC AMERICAN ONLINE
Watch a video of a rat whose memory has been wiped out at ScientificAmerican.com/may2012/forgetting

Botanists are getting a whiff of the ways that plants smell one another. Some plants recognize injured neighbors by scent; others sniff out a meal

By Daniel Chamovitz

WHAT A PLANT SMELLS

*C*USCUTA PENTAGONA IS NOT YOUR NORMAL PLANT. IT IS A SPINDLY ORANGE VINE THAT CAN GROW up to three feet high, produces tiny white flowers of five petals and is found all over North America. What is unique about *Cuscuta* [commonly known as dodder] is that it has no leaves. And it isn't green, because it lacks chlorophyll, the pigment that absorbs solar energy, allowing plants to turn light into sugars and oxygen through photosynthesis. *Cuscuta* gets its food from its neighbors. It is a parasitic plant. In order to live, *Cuscuta* attaches itself to a host plant and sucks off the nutrients provided by the host by burrowing an appendage into the plant's vascular system. What makes *Cuscuta* truly fascinating is that it has culinary preferences: it chooses which neighbors to attack.

Adapted from What a Plant Knows: A Field Guide to the Senses, *by Daniel Chamovitz, by arrangement with Scientific American/Farrar, Straus and Giroux, LLC (North America), One World (UK), Scribe (AUS/NZ), Kawade Shobo Shisha (Japan).*

A *Cuscuta* seed germinates like any other plant seed. The new shoot grows into the air, and the new root burrows into the dirt. But a young dodder left on its own will die if it doesn't quickly find a host to live off of. As a dodder seedling grows, it moves its shoot tip in small circles, probing the surroundings the way we do with our hands when we are blindfolded or searching for the kitchen light in the middle of the night. While these movements seem random at first, if the dodder is next to another plant (say, a tomato), it's quickly obvious that it is bending and growing and rotating in the direction of the to-

Illustration by Cherie Sinnen

FATAL FRAGRANCE
After smelling its way to a suitable host, a parasitic dodder vine wraps itself around a tomato plant, sucking out vital juices.

mato plant that will provide it with food. The dodder bends and grows and rotates until finally it finds a tomato leaf. But rather than touch the leaf, the dodder sinks down and keeps moving until it finds the *stem* of the tomato plant. In a final act of victory, it twirls itself around the stem, sends microprojections into the tomato's phloem (the vessels that carry the plant's sugary sap), and starts siphoning off sugars so that it can keep growing and eventually flower.

Consuelo De Moraes even documented this behavior on film. She is an entomologist at Pennsylvania State University whose main interest is understanding volatile chemical signaling between insects and plants and between plants themselves. One of her projects centered on figuring out how *Cuscuta* locates its prey. She demonstrated that the dodder vines never grow toward empty pots or pots with fake plants in them but faithfully grow toward tomato plants no matter where she put them—in the light, in the shade, wherever. De Moraes hypothesized that the dodder actually *smelled* the tomato. To check her hypothesis, she and her students put the dodder in a pot in a closed box and put the tomato in a second closed box. The two boxes were connected by a tube that entered the dodder's box on one side, thereby allowing the free flow of air between the boxes. The isolated dodder always grew toward the tube, suggesting that the tomato plant was giving off an odor that wafted through the tube into the dodder's box and that the dodder liked it.

If the *Cuscuta* was really going after the smell of the tomato, then perhaps De Moraes could just make a tomato perfume and see if the dodder would go for that. She created an *eau de tomato* stem extract that she placed on cotton swabs and then put the swabs on sticks in pots next to the *Cuscuta*. As a control, she put some of the solvents that she used to make the tomato perfume on other swabs of cotton and put these on sticks next to the *Cuscuta* as well. As predicted, she tricked the dodder into growing toward the cotton giving off the tomato smell, thinking it was going to find food, but not to the cotton with the solvents.

Given a choice between a tomato and some wheat, the dodder will choose the tomato. If you grow your dodder in a spot that is equidistant between two pots—one containing wheat, the other containing tomato—the dodder will go for the tomato.

At the basic chemical level, *eau de tomato* and *eau de wheat* are rather similar. Both contain beta-myrcene, a volatile compound (one of the hundreds of unique chemical smells known) that on its own can induce *Cuscuta* to grow toward it. So why the preference? One clear hypothesis is the complexity of the bouquet. In addition to beta-myrcene, the tomato gives off two other volatile chemicals that the dodder is attracted to, making for an overall irresistible dodder-attracting fragrance. Wheat, however, only contains one dodder-enticing odor, the beta-myrcene, and not the other two found in the tomato. What's more, wheat not only makes fewer attractants but also makes (Z)-3-Hexenyl acetate, which repels the dodder more than the beta-myrcene attracts it. In fact, the *Cuscuta* grows *away* from (Z)-3-Hexenyl acetate, finding the wheat simply repulsive.

(L)EAVESDROPPING

IN 1983 two teams of scientists published astonishing findings related to plant communication that revolutionized our understanding of everything from the willow tree to the lima bean. The scientists claimed that trees warn one another of an imminent leaf-eating-insect attack. News of their work soon spread to popular culture, with the idea of "talking trees" found in the pages not only of *Science* but of mainstream newspapers around the world.

David Rhoades and Gordon Orians, two scientists at the University of Washington, noticed that caterpillars were less likely to forage on leaves from willow trees if these trees were neighbors of other willows already infested with tent caterpillars. The healthy trees growing near the infested trees were resistant to the caterpillars because, as Rhoades discovered, the leaves of the resistant trees—but not of susceptible ones isolated from the infested trees—contained phenolic and tannin chemicals that made them unpalatable to the insects. Because the scientists could detect no physical connections between the damaged trees and their healthy neighbors—they did not share common roots, and their branches did not touch—Rhoades proposed that the attacked trees must be sending an airborne pheromonal message to the healthy trees. In other words, the infested trees signaled to the neighboring healthy trees, "Beware! Defend yourselves!"

Just three months later Dartmouth College researchers Ian Baldwin and Jack Schultz published a seminal paper that supported the Rhoades report. They studied poplar and sugar maple seedlings (about a foot tall) grown in airtight Plexiglas cages. They used two cages for their experiment. The first contained two populations of trees: 15 trees that had two leaves torn in half and 15 trees that were not damaged. The second cage contained the control trees, which of course were not damaged. Two days later the remaining leaves on the damaged trees contained increased levels of a number of chemicals that are known to inhibit the growth of caterpillars. The trees in the control cage did not show increases in any of these compounds. Baldwin and Schultz proposed that the damaged leaves, whether by tearing as in their experiments or by insect feeding as in Rhoades's observations of the willow trees, emitted a gaseous signal that enabled the damaged trees to communicate with the undamaged ones, which resulted in the latter defending themselves against imminent insect attack.

These early reports of plant signaling were often dismissed by other individuals in the scientific community as lacking the correct controls or as having correct results but exaggerated implica-

Daniel Chamovitz is director of the Manna Center for Plant Biosciences at Tel Aviv University and author of the upcoming book *What a Plant Knows*.

IN BRIEF

Plants release a bouquet of odors into the air around them. Biologists have confirmed that plants respond to one another's scents.

Some plants prepare for battle when they smell wounded neighbors, whereas the parasitic dodder vine sniffs out healthy hosts.

tions. But over the past decade the phenomenon of plant communication through smell has been shown again and again for a large number of plants, including barley, sagebrush and alder. While the phenomenon of plants being influenced by their neighbors through airborne chemical signals is now an accepted scientific paradigm, the question remains: Are plants truly communicating with one another (in other words, purposely warning of approaching danger), or are the healthy ones just eavesdropping on a soliloquy by the infested plants, not intended to be heard?

Martin Heil and his team at the Center for Research and Advanced Studies in Irapuato, Mexico, have been studying wild lima beans (*Phaseolus lunatus*) for the past several years to further explore this question. Heil knew that scientists had observed that when a lima bean plant is eaten by beetles, it responds in two ways. The leaves that are being eaten by the insects release a mixture of volatile chemicals into the air, and the flowers (though not directly attacked by the beetles) produce a nectar that attracts beetle-eating arthropods. Early in his career at the turn of the millennium, Heil had worked at the Max Planck Institute for Chemical Ecology in Jena, Germany, the same institute where Baldwin was (and still is) a director, and like Baldwin before him Heil wondered why it was that lima beans emitted these chemicals.

Heil and his colleagues placed lima bean plants that had been attacked by beetles next to plants that had been isolated from the beetles and monitored the air around different leaves. They chose a total of four leaves from three different plants: from a single plant that had been attacked with beetles they chose two leaves, one leaf that had been eaten and another that was not; a leaf from a neighboring but healthy "uninfested" plant; and a leaf from a plant that had been kept isolated from any contact with beetles or infested plants. They identified the volatile chemical in the air surrounding each leaf using an advanced technique known as gas chromatography/mass spectrometry (often featured on the show *CSI* and employed by perfume companies when they are developing a new fragrance).

Heil found that the air emitted from the foraged and the healthy leaves on the same plant contained essentially identical volatiles, whereas the air around the control leaf was clear of these gases. In addition, the air around the healthy leaves from the lima beans that neighbored beetle-infested plants also contained the same volatile chemicals as those detected from the foraged plants. The healthy plants were also less likely to be eaten by beetles.

But Heil was not convinced that damaged plants "talk" to other plants to warn them against impending attack. Rather he proposed that the neighboring plant must be practicing a form of olfactory eavesdropping on an internal signal actually intended for other leaves on the same plant.

Heil modified his experimental setup in a simple, albeit ingenious, way to test his hypothesis. He kept the two plants next to each other but enclosed the attacked leaves in plastic bags for 24 hours. When he checked the same four types of leaves as in the first experiment, the results were different. While the attacked leaf continued to emit the same chemical as it did before, the other leaves on the same vine and neighboring vines now resembled the control plant; the air around the leaves was clear.

Heil and his team opened the bag around the attacked leaf, and with the help of a small ventilator usually used on tiny microchips to help cool computers, they blew the air in one of two directions: either toward the neighboring leaves farther up the vine or away from the vine and into the open. They checked the gases coming out of the leaves higher up the stem and measured how much nectar they produced. The leaves blown with air coming from the attacked leaf started to emit the same gases themselves, and they also produced nectar. The leaves that were not exposed to the air from the attacked leaf remained the same.

The results were significant because they revealed that the gases emitted from an attacked leaf are necessary for the same plant to protect *its other leaves* from future attacks. In other words, when a leaf is attacked by an insect or by bacteria, it releases odors that warn its brother leaves to protect themselves against imminent attack, similar to guard towers on the Great Wall of China lighting fires to warn of an oncoming assault.

Given a choice between a tomato and some wheat, the dodder will choose the tomato.

The neighboring plant eavesdrops on a nearby olfactory conversation, which gives it essential information to help protect itself. In nature, this olfactory signal persists for at least a few feet (different volatile signals, depending on their chemical properties, travel for shorter or much longer distances). For lima beans, which naturally enjoy crowding, this is more than enough to ensure that if one plant is in trouble, its neighbors will know about it.

DO PLANTS SMELL?

PLANTS GIVE OFF a literal bouquet of smells. Imagine the fragrance of roses when you walk on a garden path in the summertime, or of freshly cut grass in the late spring, or of jasmine blooming at night. Without looking, we know when fruit is ready to eat, and no visitor to a botanical garden can be oblivious to the offensive odor of the world's largest (and smelliest) flower, the *Amorphophallus titanum,* better known as the corpse flower. (Luckily, it blooms only once every few years.)

Many of these aromas are used in complex communication between plants and animals. The smells induce different pollinators to visit flowers and seed spreaders to visit fruits, and as author Michael Pollan points out, these aromas can even seduce people to spread flowers all over the world. But plants don't just give off odors; as we have seen, they undoubtedly smell other plants.

Plants obviously don't have olfactory nerves that connect to a brain that interprets the signals. But *Cuscuta,* Heil's plants and other flora throughout our natural world respond to pheromones, just as we do. Plants detect a volatile chemical in the air, and they convert this signal (albeit nerve-free) into a physiological response. Surely this could be considered olfaction. SA

SCIENTIFIC AMERICAN ONLINE
For a slideshow of the plant kingdom's most unusual talents, visit ScientificAmerican.com/may2012/what-plants-smell

FORENSIC MEDICINE

TELLTALE HEARTS

Despite advances in medical imaging, an autopsy still gives experts the best picture of what ails us

By Ann Chin

THE HUMAN HEART ENDURES A LOT IN a lifetime. Sophisticated imaging can give insight into what it tolerates and what ails it, but the most direct information comes from an autopsy.

Photographer Angela Strassheim spent days at an undisclosed morgue in 2000, capturing the organ moments after its removal. She left with a series of images that show (*clockwise from lower left*) hearts pierced by a gunshot wound, damaged by obesity, affected by cancer and weakened by a drug overdose. In the center is a child's healthy heart. The photographs are being published here for the first time.

Comparing the hearts of healthy and obese individuals demonstrates how the latter get remodeled in unhealthy ways. Michael Lauer of the National Heart, Lung, and Blood Institute says research suggests that fat exerts toxic effects not only on the coronary arteries but on the heart muscle itself. In the image, fat visibly surrounds the organ, and the muscle is enlarged. The effects of drugs and of cancer that spreads to the heart are less visible here; both conditions can alter valve function and blood flow.

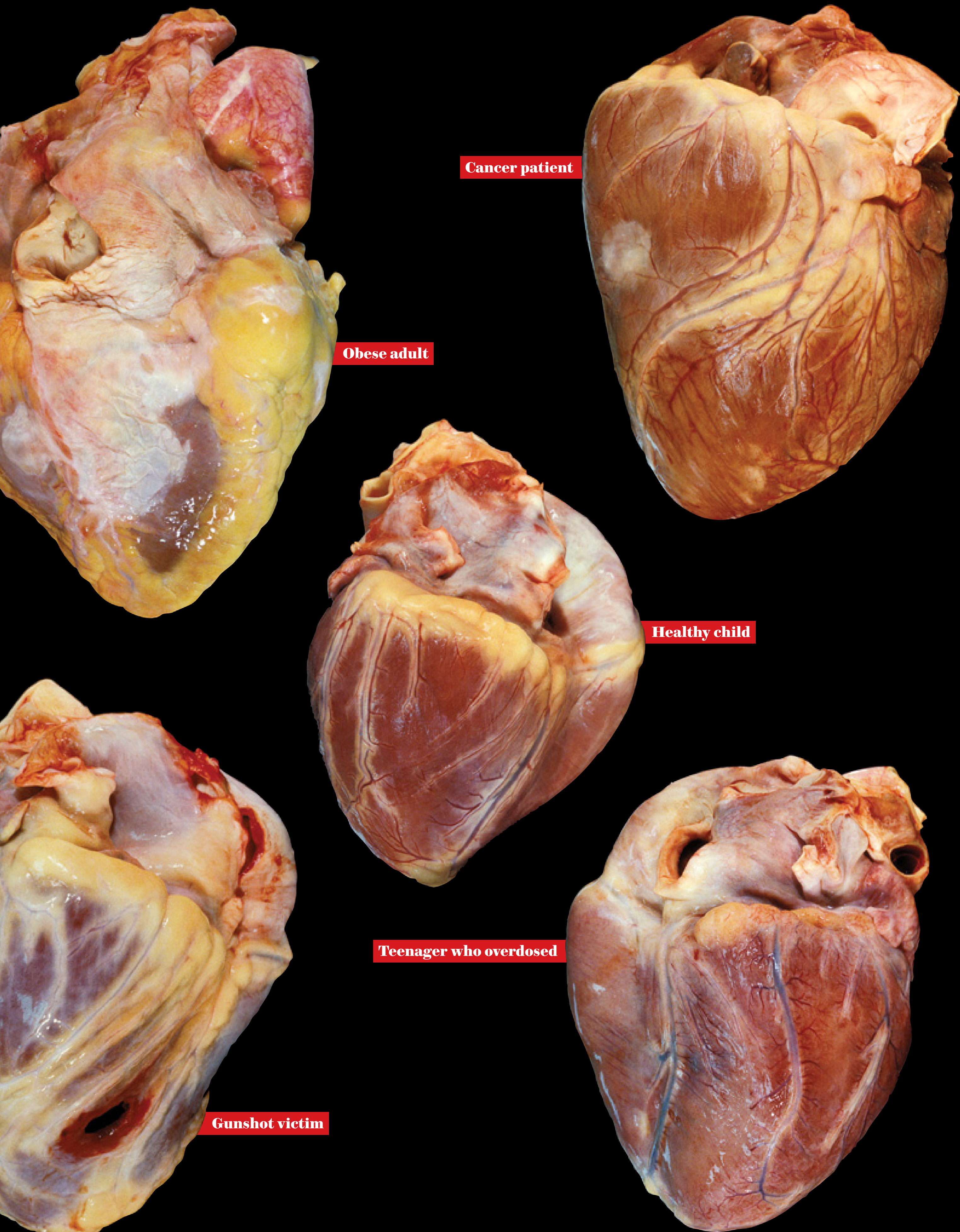
Despite their importance for research, autopsies are on the decline. The U.S. Centers for Disease Control and Prevention report that rates dropped by more than 50 percent between 1972 and 2007 because of such factors as changes in state laws that govern which deaths can be investigated, as well as a lack of insurance coverage for the procedure.

Although there have been advances in postmortem imaging, the technology has failed to diagnose some instances of heart disease and cancer. In an *Annals of Internal Medicine* editorial earlier this year, Elizabeth Burton and Mahmud Mossa-Basha of Johns Hopkins University said that until imaging technologies improve, "autopsy remains the gold standard for determining the cause of death." SA

Ann Chin *is assistant photo editor for* Scientific American.

SCIENTIFIC AMERICAN ONLINE
For more on these images, see ScientificAmerican.com/may2012/autopsy

ANGELA STRASSHEIM


Cancer patient
Obese adult
Healthy child
Teenager who overdosed
Gunshot victim

METEOROLOGY

A BETTER EYE

ON THE STORM

New technology that increases the warning time for tornadoes and hurricanes could potentially save hundreds of lives every year

By Jane Lubchenco and Jack Hayes

AFTER THE DEAFENING ROAR OF A THUNDERSTORM, an eerie silence descends. Then the blackened sky over Joplin, Mo., releases the tentacles of an enormous, screaming multiple-vortex tornado. Winds exceeding 200 miles per hour tear a devastating path three quarters of a mile wide for six miles through the town, destroying schools, a hospital, businesses and homes and claiming roughly 160 lives.

Nearly 20 minutes before the twister struck on the Sunday evening of May 22, 2011, government forecasters had issued a warning. A tornado watch had been in effect for hours and a severe weather outlook for days. The warnings had come sooner than they typically do, but apparently not soon enough. Although emergency officials were on high alert, many local residents were not.

IN BRIEF

Stronger or more frequent weather extremes will likely occur under climate change, such as more intense downpours and stronger hurricane winds.

Improved weather prediction, therefore, will be vital to giving communities more time to prepare for dangerous storms, saving lives and minimizing damage to infrastructure.

New radar technology will allow forecasters to better "see" extreme weather, as will potential improvements to satellite technology, as well as computer models that run on more powerful supercomputers.

Longer warning time is only effective when paired with better understanding of how to get people to respond to the warnings, all part of an effort to build a "weather-ready nation."

The Joplin tornado was only one of many twister tragedies in the spring of 2011. A month earlier a record-breaking swarm of tornadoes devastated parts of the South, killing more than 300 people. April was the busiest month ever recorded, with about 750 tornadoes.

At 550 fatalities, 2011 was the fourth-deadliest tornado year in U.S. history. The stormy year was also costly. Fourteen extreme weather and climate events in 2011—from the Joplin tornado to hurricane flooding and blizzards—each caused more than $1 billion in damages. The intensity continued early in 2012; on March 2, twisters killed more than 40 people across 11 Midwestern and Southern states.

Tools for forecasting extreme weather have advanced in recent decades, but researchers and engineers at the National Oceanic and Atmospheric Administration are working to enhance radars, satellites and supercomputers to further lengthen warning times for tornadoes and thunderstorms and to better determine hurricane intensity and forecast floods. If the efforts succeed, a decade from now residents will get an hour's warning about a severe tornado, for example, giving them plenty of time to absorb the news, gather family and take shelter.

Jane Lubchenco has been NOAA Administrator since 2009. She is a marine ecologist and environmental scientist, with expertise in oceans, climate change and interactions between the environment and human well-being.

John L. "Jack" Hayes is director of the National Weather Service at NOAA. He is responsible for the preparation and delivery of weather warnings and predictions to government, industry and the general public.

THE POWER OF RADAR

METEOROLOGIST DOUG FORSYTH is heading up efforts to improve radar, which plays a role in forecasting most weather. Forsyth, who is chief of the Radar Research and Development division at NOAA's National Severe Storms Laboratory in Norman, Okla., is most concerned about improving warning times for tornadoes because deadly twisters form quickly and radar is the forecaster's primary tool for sensing a nascent tornado.

Radar works by sending out radio waves that reflect off particles in the atmosphere, such as raindrops or ice or even insects and dust. By measuring the strength of the waves that return to the radar and how long the round-trip takes, forecasters can see the location and intensity of precipitation. The Doppler radar currently used by the National Weather Service also measures the frequency change in returning waves, which provides the direction and speed at which the precipitation is moving. This key information allows forecasters to see rotation occurring inside thunderstorms before tornadoes form.

In 1973 NOAA meteorologists Rodger Brown, Les Lemon and Don Burgess discovered this information's predictive power as they analyzed data from a tornado that struck Union City, Okla. They noted very strong outbound velocities right next to very strong inbound velocities in the radar data. The visual appearance of those data was so extraordinary that the researchers initially did not know what it meant. After matching the data to the location of the tornado, however, they named the data "Tornadic Vortex Signature." The TVS is now the most important and widely recognized metric indicating a high probability of either an ongoing tornado or the potential for one in the very near future. These data enabled longer lead times for tornado warnings, increasing from a national average of 3.5 minutes in 1987 to 14 minutes today.

Although Doppler radar has been transformative, it is not perfect. It leaves meteorologists like Forsyth blind to the shape of a given particle, which can distinguish, say, a rainstorm from a dust storm. Ironically, the trajectory of his career path changed when a failed eye exam led him from U.S. Air Force pilot ambitions to a career in meteorology. Since then, Forsyth has focused on radar upgrades that give forecasters a better view of the atmosphere.

One critical upgrade is called dual polarization. This technology allows forecasters to differentiate more confidently between types of precipitation and amount. Although raindrops and hailstones may sometimes have the same horizontal width—and therefore appear the same in Doppler radar images—raindrops are flatter. Knowing the difference in particle shape reduces the guesswork required by a forecaster to identify features in the radar scans. That understanding helps to produce more accurate forecasts, so residents know they should prepare for hail and not rain, for example.

Information about particle size and shape also helps to distinguish airborne bits of debris lofted by tornadoes and severe thunderstorms, so meteorologists can identify an ongoing damaging storm. Particle data are especially important when trackers are dealing with a tornado that is invisible to the human eye. If a tornado is cloaked in heavy rainfall or is occurring at night, dual polarization can still detect the airborne debris.

The National Weather Service is integrating dual-polarization technology—which is also helpful for monitoring precipitation in hurricanes and blizzards—into all 160 Doppler radars across the nation, expecting to finish by mid-2013. At the same time, NOAA personnel are training forecasters to interpret the new images. The Weather Forecast Office in Newport/Morehead City, N.C., was the first to scan a tropical cyclone using such radar when Hurricane Irene made landfall in North Carolina in 2011. During that storm, dual-polarization radars proved more accurate in detecting precipitation rates, and therefore predicting flooding, than conventional Doppler radars farther north. The improved capabilities surely saved lives in the Carolinas; farther up the coast, without this technology, Hurricane Irene was deadlier despite early warnings, claiming nearly 30 lives.

NOAA research meteorologist Pam Heinselman believes another advanced radar technology used by the U.S. Navy to detect and track enemy ships and missiles has great potential to improve weather forecasting as well. Heinselman leads a team of electrical engineers, forecasters and social scientists at the National Weather Radar Testbed in Norman, Okla., focused on a technology called phased-array radar.

Current Doppler radars scan at one elevation angle at a time, with a parabolic dish that is mechanically turned. Once the dish completes a full 360-degree slice, it tilts up to sample another small sector of the atmosphere. After sampling from lowest to highest elevation, which during severe weather equates to 14 in-

DAVID MAYHEW *(preceding pages)*

dividual slices, the radar returns to the lowest angle and begins the process all over again. Scanning the entire atmosphere during severe weather takes Doppler radar four to six minutes.

In contrast, phased-array radar sends out multiple beams simultaneously, eliminating the need to tilt the antennas, decreasing the time between scans of storms to less than a minute. The improvement will allow meteorologists to "see" rapidly evolving changes in thunderstorm circulations and, ultimately, to more quickly detect the changes that cause tornadoes. Heinselman and her team have demonstrated that phased-array radar can also gather storm information not currently available, such as fast changes in wind fields, which can precede rapid changes in storm intensity.

Heinselman and others believe phased-array technology alone could extend tornado warnings to more than 18 minutes, but much more research and development needs to be done. Ideally, the phased-array system would have four panels that emitted and received radio waves, to provide a 360-degree view of the atmosphere—one each for the north, south, east and west. Researchers in Norman have made only one-panel systems operable for weather surveillance, and it is likely to be at least a decade before phased arrays become the norm across the country.

EYES IN THE SKY

OF COURSE, even the best radars cannot see over mountains or out into the oceans, where hurricanes form. Forecasters rely on satellites for these situations and also rely on them to provide broader data that supplement the localized information from a given radar. NOAA's weather satellites supply more than 90 percent of the data that go into daily and long-range forecasts, and they are critical in providing alerts of severe weather potential multiple days in advance. To improve the delivery of this essential environmental intelligence, NOAA will deploy a range of new technologies in the next five years.

Without more detailed satellite observations, extending the range of accurate weather forecasts—especially for such extreme events as hurricanes—would be severely restricted. Monitoring weather requires two types of satellites: geostationary and polar-orbiting. Geostationary satellites, which stay fixed in one spot at an altitude of about 22,000 miles, transmit near-continuous views of the earth's surface. Using loops of pictures taken

SCIENCE AND SOCIETY

Fair Warning

Many people died in the May 2011 tornadoes that struck Joplin, Mo., because the weather was so intense, but fewer deaths would have occurred if more people had found a secure shelter sooner. NOAA social scientist Vankita Brown worked with the National Weather Service's research teams to identify what could have been done to spur better public action. They discovered that many people did not act after they heard the first siren or tornado warning but waited until they had confirmation from other sources, including friends. After such confirmation they were more likely to seek shelter. Others simply did not take the risk seriously enough.

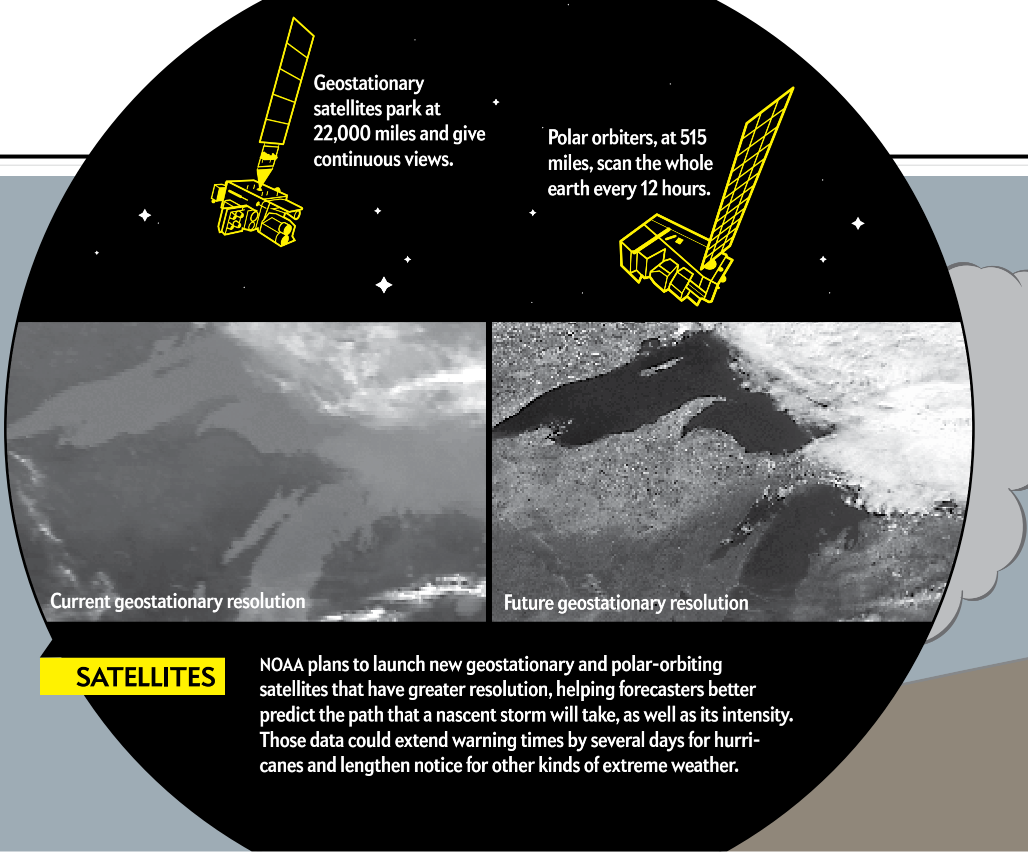
As Brown explains, people typically do not think that low-frequency, high-impact events such as tornadoes and hurricanes will happen to them. Perceptions of "being safe" change to "being at risk" only immediately after a community-wide disaster occurs. Presented with this kind of moment after the Joplin tornado, NOAA called for a national dialogue on how to build a "weather-ready nation."

Analysis arising from various scientific meetings highlights a number of steps that can persuade more people to act on warnings. Forecasters on radio and TV can show the exact location of a storm that is about to break. Because individuals are more likely to take action if they see family members or friends acting, those who are preparing for a storm can use Facebook or Twitter to motivate others. NOAA can encourage that behavior by posting its own Facebook and Twitter updates, which is being tested now, and by highlighting warnings online in Google maps. The Federal Emergency Management Agency and the Federal Communications Commission have also begun to broadcast messages from every cellular tower to all cell phones in range. Paired with earlier warnings, such actions may help minimize tragedy. *—J.L. and J.H.*

AP PHOTO/AERIAL IMAGERY COURTESY OF MJ HARDEN, A GEOEYE COMPANY

Improving Weather Prediction

Predicting storms has come a long way. Forecasters can now give U.S. residents an average of 14 minutes of warning before a tornado strikes, for example. Yet upcoming technology improvements from the National Oceanic and Atmospheric Administration may extend warning time significantly for all kinds of extreme weather.



at 15-minute intervals, forecasters can monitor rapidly growing storms or detect changes in hurricanes (but not tornadoes).

Polar satellites, which orbit the earth from pole to pole at an altitude of approximately 515 miles, give closer, more detailed observations of the temperature and humidity of different layers of the atmosphere. A worldwide set of these low Earth orbit (LEO) satellites covers the entire globe every 12 hours.

NOAA plans to launch a new series of LEO satellites this decade, as part of the Joint Polar Satellite System, with updated hardware, fitted with more sophisticated instruments. Their data will be used in computer models to improve weather forecasts, including hurricane tracks and intensities, severe thunderstorms and floods. The suite of advanced microwave and infrared sensors will relay much improved three-dimensional information on the atmosphere's temperature, pressure and moisture, because rapid changes in temperature and moisture, combined with low pressure, signify a strong storm. Infrared sensors provide these measurements in cloud-free areas, and microwave sensors can "see through clouds" to the earth's surface.

In April 2011, five days before a powerful storm system tore through six southern states, NOAA's current polar-orbiting satellites provided data that, when fed into models, prompted the NOAA Storm Prediction Center to forecast "a potentially historic tornado outbreak." The center elevated the risk to the highest level at midnight before the event. This level of outlook is reserved for the most extreme cases, with the least uncertainty, and is only used when the possibility for extremely explosive storms is detected. The new LEO satellites should allow such predictions as much as five to seven days before a storm.

Geostationary satellites will improve, too. Advanced instruments that will image the earth every five minutes in both visible and infrared wavelengths will be onboard the GOES-R series of satellites to be launched in 2015. They will increase observations from every 15 minutes to every five minutes or less, allowing scientists to monitor the rapid intensification of severe storms. The GOES-R satellites will also provide the world's first space view of where lightning is occurring in the Western Hemisphere. The lightning mapper will help forecasters detect jumps in the frequency of in-cloud and cloud-to-ground lightning flashes. Research suggests that these jumps occur up to 20 minutes or more before hail, severe winds and even tornadoes.

BILLIONS OF DATA

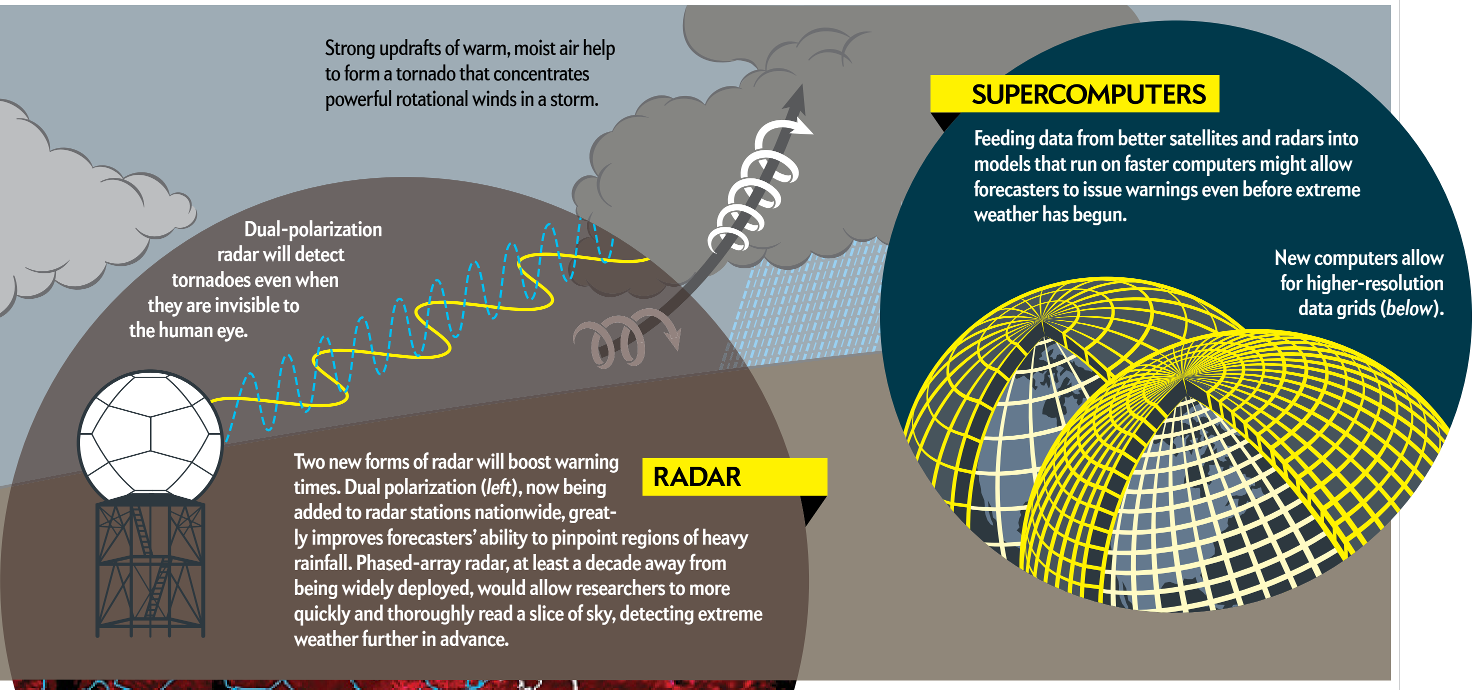
EACH OF THE NEW RADAR TECHNOLOGIES and satellites could improve warning times by several minutes, but incorporating the data derived from all these systems into forecasting computer models could provide even more time. Warnings for tornadoes, for example, could be issued up to an hour in advance. That is the kind of lead time that would have made a big difference in Joplin.

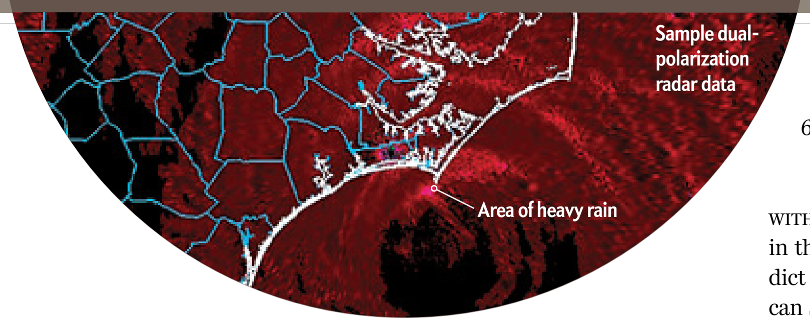
Forecasting models are based on physical laws governing atmospheric motion, chemical reactions and other relationships. They crunch millions of numbers that represent current weather and environmental conditions, such as temperature, pressure and wind, to predict the future state of the atmosphere. Imagine a grid that lies over the planet's surface. Imagine another one a few hundred feet above that—and another and another, in layer after layer, all the way to the top of the stratosphere some 30 miles up. Millions of lines of code are needed to translate the billions of grid points under observation.

A typical forecast model today uses grids at the surface that run about five to 30 miles square. The smaller the squares, the higher the model's resolution and the better it will be at detecting small-scale atmospheric changes that could spawn storms. Processing more data points, however, requires faster supercomputers.

Advances in modeling also require talented people who can integrate all these data and interpret them. Bill Lapenta, acting director of NOAA's Environmental Modeling Center, heads that translation effort, which churns out numerical forecasts for 12, 24,

COURTESY OF NOAA (*maps*)





36, 48 and 72 hours ahead and beyond. Meteorologists compare NOAA's models with others from international modeling centers to come up with the forecasts seen on the Web or the evening news.

NOAA supercomputers in Fairmont, W.Va., can process 73.1 trillion calculations a second. But Lapenta believes faster speeds are possible, which will allow the models to run at even smaller scales. For example, grids of just one mile square would enable models to simulate the small-scale conditions that catapult a routine thunderstorm or hurricane into a monster. NOAA plans to access some of the latest supercomputers at Oak Ridge National Laboratory to begin to build such models. Lapenta hopes such high-resolution models might begin to appear by 2020.

Lapenta foresees a day in the next decade when the increasing capabilities of new radars and satellites will be coupled with an evolving generation of finely detailed weather-prediction models running in real time on computers at speeds exceeding a quintillion computations a second. To make them a reality, scientists such as Lapenta are working on the mathematical, physical and biogeochemical relations that need to be encoded in a way that enables those relations to work together seamlessly.

If major NOAA investments in this "brainware" pay off, forecasters will not have to wait for a radar image to detect an actual storm before issuing a warning with 14 or 18 minutes of lead time. Instead they will be able to issue tornado, severe thunderstorm and flash-flood warnings based on highly accurate model forecasts produced well in advance, giving the public 30 to 60 minutes to take safety precautions.

BETTER SCIENCE, BETTER DECISIONS

WITH ALL THESE IMPROVEMENTS, meteorologists such as Gary Conte in the New York City Weather Forecast Office will be able to predict more accurately, with longer lead times, weather hazards that can shut down the city, such as storms with snow and ice. Severe weather outlooks will extend beyond five days, hurricane forecasts beyond seven days, and the threat of spring floods will be known weeks in advance. This vision for a weather-ready nation is motivated by the desire to avoid the unmitigated disasters of 2011.

The goal is that by 2021 the rebuilt and thriving city of Joplin would receive a severe tornado warning more than an hour in advance. Families would have more time to gather and get to a safe room. Nursing homes and hospitals would be able to transfer residents and patients to shelter. Retailers would have time to get employees to safety and close up shop. Cell phones would thrum with multiple messages to seek shelter while local meteorologists broadcast similar warnings on television and radio. The clarion call of tornado sirens would reinforce the urgency of these warnings. As a result, even nature's most powerful tornado would pass through town without any loss of life. SA

MORE TO EXPLORE

NOAA National Weather Service: **http://weather.gov**

NOAA Storm Prediction Center: **www.spc.noaa.gov**

Managing the Risks of Extreme Events and Disasters to Advance Climate Change Adaptation. Special IPCC report. Edited by C. B. Field et al. Cambridge University Press (in press).

SCIENTIFIC AMERICAN ONLINE
For a video of NOAA's effort to cope with extreme weather, visit **ScientificAmerican.com/may2012/weather**

Illustration by Jameson Simpson

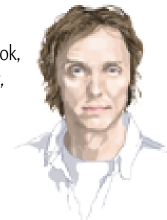
PHOTONICS

NATURE'S COLOR TRICKS

Understanding seven clever tactics animals use to create dazzling hues may lead to sophisticated new technologies

By Philip Ball

Philip Ball is a science writer in London. His latest book, *Curiosity: How Science Became Interested in Everything,* was published by Bodley Head this month.



THE CHANGING HUES OF A PEACOCK'S SPLENDID TAIL FEATHERS have always captivated curious minds. Seventeenth-century English scientist Robert Hooke called them "fantastical," in part because wetting the feathers caused the colors to disappear. Hooke used the recently invented microscope to investigate the feathers and saw that they were covered with tiny ridges, which he figured might produce the brilliant yellows, greens and blues.

Hooke was on the right track. The intense colors of bird plumages, butterfly wings and the bodies of squid are often produced not by light-absorbing pigments but by arrays of tiny structures that are just a few hundred nanometers wide. The size and spacing of these structures pick out particular wavelengths from the full spectrum of sunlight. The hues are also often iridescent, changing, like magic, from blue to green or orange to yellow, depending on the angle at which we see the animal. And because the colors are produced just by reflecting light rather than absorbing some of it, as pigments do, they can be more brilliant. The blue morpho butterfly of South and Central America can be seen from up to a kilometer away; it seems to shine when sunlight penetrates a tropical forest canopy and bounces off its wings.

Scientists are beginning to understand more fully how the delicately arranged nanostructures of living organisms manipulate light, which in turn is inspiring engineers to mimic the biological designs in new, man-made optical materials. The materials could lead to more brilliant visual displays and new chemical sensors, as well as to better storage, transmission and processing of information.

We know relatively little about how these biological structures evolved, but we are at least learning how they are formed and how they produce fantastical colors. Nature does not have sophisticated technologies such as electron beams that can etch thin layers of material, so it has relied on ingenuity instead. If engineers can master the same art, they might develop cheap fabrics that change appearance like the camouflage of squid or like computer chips that transmit information optically instead of electrically and at blazing speeds. Here we look at some of nature's tricks for forming structures that create color and the ways inventors are trying to exploit them.

IN BRIEF

Birds, butterflies, squid and other creatures often sport intense or changing colors that are not formed by pigments but by highly organized nanostructures that researchers are only beginning to unravel.

Orderly and disorderly geometric patterns of these nanostructures reflect only certain wavelengths of light, creating specific colors that in some cases can also shift if the structures get wet or if their dimensions change.

Scientists are making synthetic materials that mimic these biological structures, which could lead to cars or dresses that change color as they move, sensors that detect impurities in drinking water, efficient optical chips for cell phones and authentication marks on credit cards that are exceedingly hard to counterfeit.

GETTY IMAGES *(preceding pages)*

1 LAYERS ON LAYERS

The ridges Hooke discovered on peacock feathers do scatter light, but the bright colors generally come from nanostructures he could not see that lie underneath the surface. The colored feathers of birds and scales of fish and butterflies typically contain microscopic, organized layers or rods of a dense light-scattering material. Because the distance between the layers or rods is roughly the same as the wavelengths of visible light, the structures cause the phenomenon known as diffraction. Incoming light rays of certain wavelengths reflect off the layers and interfere with one another "constructively" or "destructively," boosting some colors in the reflected light while canceling others. The same process creates the rainbow of colors seen when the shiny surface of a compact disc is tilted back and forth.

In butterfly wings, the reflecting layers are made of the natural polymer chitin, separated by air-filled voids within the hard outer surface (cuticle) of the wing scales. In bird feathers, the layers or rods are made of melanin and embedded in keratin, the protein that makes up our hair and fingernails. The optics industry already uses diffraction gratings made from ultrathin, alternating layers of two materials to select and reflect light of a single color in products ranging from telescopes to solid-state lasers.

The male Lawes's parotia (*Parotia lawesii*) bird of paradise employs an ingenious twist on this trick, which Doekele G. Stavenga of the University of Groningen in the Netherlands discovered in 2010. Hairlike barbules on its breast feathers contain layers of melanin spaced at a distance that creates bright orange-yellow reflections. But each barbule has a V-shaped cross section with sloping surfaces that also reflect blue light. Slight movements of the feathers during the bird's courtship ritual can switch the color abruptly between orange-yellow and blue-green, a change guaranteed to catch a female's eye.

Technologists have not tried to mimic the effect, but Stavenga imagines that the fashion and automobile industries will eventually try to exploit these color changes. V-shaped microflakes in fabric could make a dress change color as the wearer moves, and such microflakes in paint could make the color of a passing car morph dramatically.

IRIDESCENT blue-green feathers of the Lawes's parotia bird of paradise can abruptly switch to yellow when slight movements alter the positioning of barbules on the feather tips (*above*).

2 THE CHRISTMAS TREE EFFECT

The butterflies *Morpho didius* and *M. rhetenor* obtain their dazzling blue color not from multilayers of chitin but from more complex nanostructures in the wing scales: arrays of chitin that are shaped like Christmas trees and sprout at the scales' outward surface. The parallel branches of each "tree" act as another kind of diffraction grating. These arrays may reflect up to 80 percent of the incident blue light. And because they are not flat, they can reflect a single color over a range of viewing angles, somewhat reducing the iridescence. Organisms do not always want to change color when seen from different directions.

As Hooke observed with peacock feathers, when water runs over the blue morpho's wings, it changes the refraction of the light. Different liquids that have different indexes of refraction therefore lead to different color reflections. Researchers at GE Global Research in Niskayuna, N.Y., in collaboration with others at the University at Albany and butterfly wing expert Pete Vukusic of the University of Exeter in England, are developing artificial *Morpho*-like structures to create chemical sensors that can identify a range of different liquids, taking on a unique color depending on the liquid they come into contact with. They use microlithographic techniques borrowed from the semiconductor industry to carve the structures into solids. The sensors could possibly detect certain emissions at power plants or impurities in drinking water.

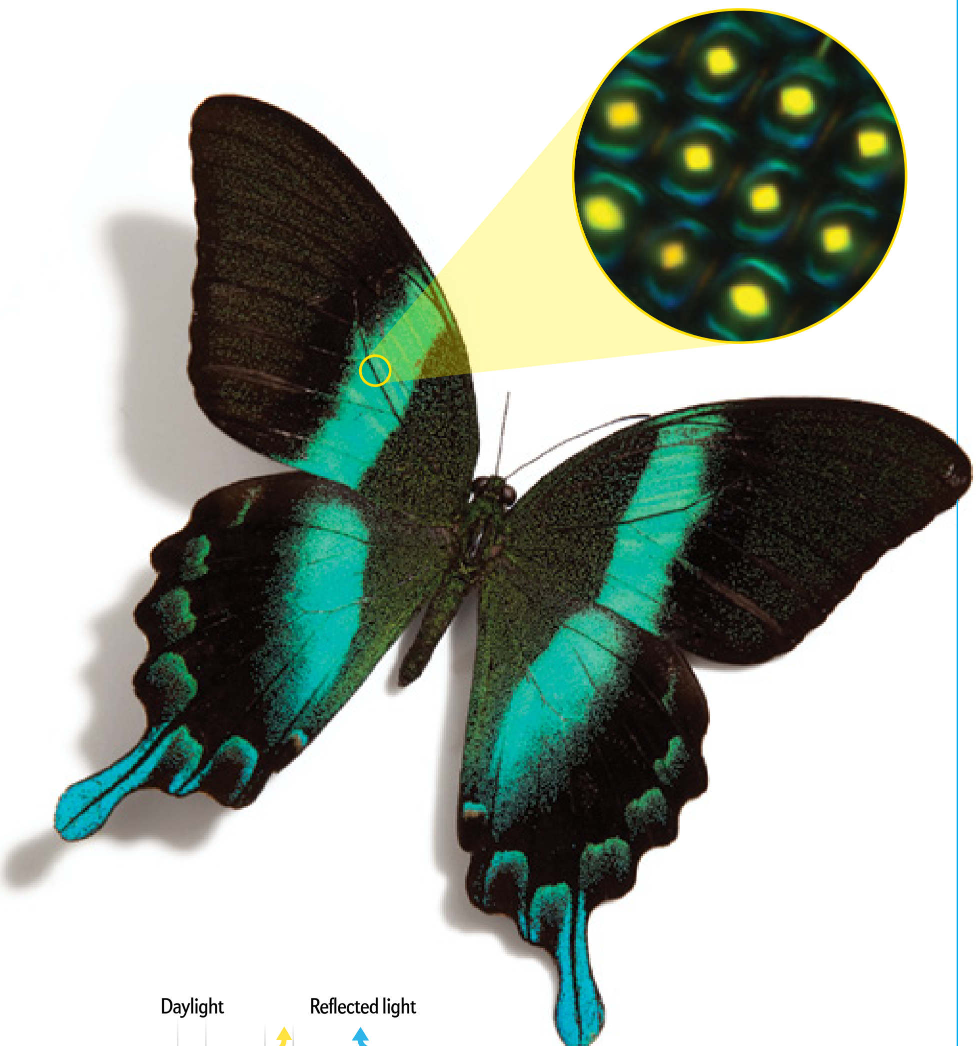
3 LIGHT-BOUNCING BOWLS

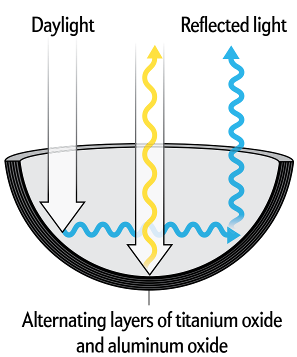
The bright-green color of the emerald swallowtail butterfly (*Papilio palinurus*), found widely in Southeast Asia, is not produced by green light at all. The wing scales are covered with a grid of tiny, bowl-shaped dimples just a few microns across. The dimples are lined with layers of chitin separated by air, which act as selective mirrors. The bottoms of the bowls reflect only yellow light, and the sides of the bowls surrounding the yellow center reflect only blue. Our eyes cannot resolve the yellow and blue at such small scales, so our brain sees the combination as green.

Christopher Summers and Mohan Srinivasarao of the Georgia Institute of Technology have copied this method for making color. To create the tiny bowls, they let

JOHN MASON *Ardea* (bird); COURTESY OF DOEKELE G. STAVENGA *University of Groningen* (close-up) water vapor condense as microscopic droplets on the surface of a polymer that is setting from liquid to solid. The water droplets pack together on the surface like rows of eggs in a carton, sinking into the film. The droplets evaporate as the polymer sets, creating a surface that has bowl-like dimples. The researchers then deposit thin, alternating layers of titanium oxide and aluminum oxide in each bowl to make a reflector that mimics the natural lining of the butterfly bowls.

Light bouncing off the patterned film appears green. When the film is placed under a set of polarizing filters, however, the yellow light bouncing back from the centers of the bowls disappears while the blue light from the rims remains. This mechanism could offer a distinctive authentication mark on credit cards and bank cards. What would appear as a simple green reflective coating would in fact carry a hidden, polarized yellow and blue signature that would be difficult to counterfeit. Srinivasarao admits, though, that the main reason they are trying to replicate the butterfly's green color is that "it's beautiful in its own right."





BOWLED GREEN: The emerald swallowtail butterfly's hue comes from a mix of blue and yellow reflections from tiny bowl-like depressions in the wing scales (*inset above*). A nanostructure (*left*) made at the Georgia Institute of Technology to mimic the effect could work as a watermark on credit cards that is hard to counterfeit.

MONICA STEVENSON *Getty Images (butterfly)*; COURTESY OF MOHAN SRINIVASARAO *Georgia Institute of Technology (wing inset)*

4 NANOSPONGES

Another butterfly, the emerald-patched cattleheart (*Parides sesostris*), creates green color by using a different nanostructure; again, no pigments are involved. Its wing scales sport microscopic, crystalline arrays of holes. These so-called photonic crystals totally exclude light within a particular band of wavelengths, causing that light to reflect. Opal gemstones are photonic crystals made from tiny spheres of stacked-together silica that scatter light, thus giving the stone its iridescent rainbow colors. Photonic crystals can be used to confine light within narrow channels, creating waveguides that could possibly steer light around the tight spaces on computer chips.

Under the electron microscope, the cattleheart butterfly's wing scales display arrays with a zigzagging appearance—patches of sponge made from chitin with orderly patterns of holes that are around 150 nanometers or so across. Each patch is a photonic crystal set at a slightly different angle from its neighbors. The structure enables it to reflect light within the green part of the spectrum over a wide range of incident angles. Some weevils and other beetles also derive their iridescent color from photonic crystals made of chitin.

Biologist Richard Prum of Yale University and his colleagues have figured out how these photonic crystals grow as young butterfly wings develop. Essentially lipids in the embryonic wing-scale cells spontaneously form a patterned template in three dimensions, and chitin hardens around them. The lipids then break down as the cells die, leaving a hollow matrix with a regular pattern of voids.

Researchers are trying to make similar structures from scratch. For instance, lipid-like molecules called surfactants will form orderly sponges, as will so-called block copolymers. Ulrich Wiesner of Cornell University has used these copolymers to arrange nanoparticles of niobium and titanium oxide into mineral-like "nanosponge" structures.

These porous solids could find a wide range of applications, such as more efficient, low-cost solar cells. Moreover, Wiesner has calculated that nanosponges made from metals such as silver or aluminum could have the weird property of a negative index of refraction, meaning they would bend light "the wrong way." Such materials, if they can be fabricated, could form superlenses for optical microscopes that can image objects smaller than the wavelength of light, which is not possible in conventional microscopes.

5 CRYSTAL FIBERS

Animals can sculpt photonic crystals in many ways. The spines of some marine worms, such as *Aphrodita* (the sea mouse), contain hexagonal arrays of hollow fibers a few hundred nanometers across. These arrays, made from chitin, exclude light in the red part of the spectrum, giving the *Aphrodita* spine an iridescent red color.

It is not clear if these optical properties have any biological function in the sea mouse. But applications in optical technology certainly exist for such light-manipulating fibers. Philip Russell, now at the Max Planck Institute for the Science of Light in Erlangen, Germany, has heated and drawn out bundles of glass capillaries into thin fibers laced with hexagonally packed holes. If a wider capillary or a solid rod is added into the middle of the original bundle, it creates a defect in the array of holes, along which light can pass while being excluded from the surrounding photonic crystal. This creates an optical fiber with a cladding that is essentially impermeable to light within a particular band of wavelengths.

Photonic crystal fibers "leak" less light than conventional ones, so they could replace the standard fibers in telecommunications networks. They would require less power, thereby eliminating the need for costly amplifiers to boost signals sent over long distances. Conventional fibers become particularly leaky at tight bends, where the reflections that confine the light inside the fiber are less efficient. Photonic crystals do not have this problem, because their light trapping does not rely on reflection. Thus, they should work better in small, confined spaces, resulting in optical microchips that are far faster than the electronic chips in our computers and cell phones.

6 DEFORMED MATRICES

To create colors, some creatures form spongy matrices that have a disorderly pattern instead of an orderly one. This structural variation creates the splendid blue and green plumage of many birds that lacks the iridescence seen on the hummingbird or the peacock. Because the spongelike keratin nanostructures in these cases are disordered, the light scattering is diffuse, akin to the blue of the sky, rather than mirrorlike and iridescent, so the color appears uniform when viewed from any angle.

In the blue and yellow macaw (*Ara ararauna*) and the black-capped kingfisher (*Halcyon pileata*), the empty spaces in the matrix of the feather barbs form tortuous channels about 100 nanometers wide. A similar random network in the cuticle of the *Cyphochilus* beetle gives it a dazzlingly bright white shell. In the blue-crowned manakin (*Lepidothrix coronata*), the airholes are not channels but are little, connected bubbles.

Yale's Prum thinks the channels or bubbles are created as keratin separates spontaneously, like oil from water, from the fluid in feather-forming cells during early development. He also thinks that birds have evolved a way to control the rate at which the keratin separates, so the channel or bubble formation stops when the voids reach a certain size. This size determines the wavelength of scattered light and thus the feather's color.

Diffuse light scattering can be seen in other natural and man-made substances. In milk, microdroplets of fat with a wide size range scatter all visible wavelengths, thus creating an opaque whiteness.

Exeter's Vukusic has mimicked the *Cyphochilus* beetle cuticle with random porous matrices of calcium carbonate or titanium dioxide mixed with a polymer, making thin coatings that are brilliantly white. Meanwhile Prum and bioengineer Eric Dufresne, also at Yale, have imitated the disordered sponges of bird feathers by creating films of randomly packed microscopic polymer beads, which have blue-green colors. These approaches could lead to coatings that have strong, highly opaque colors even though they are extremely thin, and the colors would never fade because the films do not contain organic pigments.

7 REVERSIBLE PROTEINS

One of nature's most enviable optical tricks is to produce reversible color changes. Squid in the Loliginidae family use a protein called reflectin to create and alter colors in their skin. The protein molecules are arranged into stacks of plates inside cells called iridophores, which reflect specific colors. Biologists think the color changes serve as camouflage and as communication for mating and displays of aggression.

Daniel Morse of the University of California, Santa Barbara, is studying how iridophores change color. The reflectin proteins crumple into nanoparticles, which form the plates. The plates are sandwiched between folds in the iridophore cell's membrane. When a neurotransmitter activates a biochemical process that neutralizes the electrical charge of the reflectins, the proteins pack more closely. The change increases the reflectivity of the plates and changes their spacing, altering the color. The change can be reversed if the reflectins regain charge.

Morse thinks he can mimic this mechanism in optical devices, perhaps using reflectins themselves. His team has inserted the gene that encodes a reflectin protein in the longfin inshore squid *Loligo pealeii* into *Escherichia coli* bacteria. When expressed, the protein collapses into nanoparticles. The particle size can be tuned with salts that control the interactions between charges on the proteins. The materials might then swell and contract, altering the reflected wavelengths in response to chemical triggers.

Morse has also developed a polymer that dramatically switches from transparent to opaque in response to electrical voltages, which alter the polymer's reflectivity and swell the polymer film by drawing in salt. Devices using these materials can be made with simple, low-tech manufacturing methods. His team is working with Raytheon Vision Systems in Goleta, Calif., to turn this material into fast shutters for infrared cameras, thus enabling high-speed "night filming" by detecting heat rather than light. ■

MORE TO EXPLORE

Photonic Structures in Biology. Pete Vukusic and J. Roy Sambles in *Nature,* Vol. 424, pages 852–855; August 14, 2003.

Natural Photonics. Pete Vukusic in *Physics World,* Vol. 17, No. 2, pages 35–39; February 2004.

Optical Filters in Nature. H. D. Wolpert in *Optics and Photonics News,* Vol. 20, No. 2, pages 22–27; February 2009.

A Protean Palette: Colour Materials and Mixing in Birds and Butterflies. Matthew D. Shawkey et al. in *Journal of the Royal Society Interface,* Vol. 6, Supplement No. 2, pages S221–S231; April 6, 2009.

SCIENTIFIC AMERICAN ONLINE
For images of iridescent paintings that change color, created with nanoparticle paints by artist Franziska Schenk, see **ScientificAmerican.com/may2012/schenk**

INNOVATION

Professional Seer

The world's largest computer chipmaker employs a corporate futurist, Brian David Johnson, to guess what gadgetry and computing will look like in 2020 and beyond

Interview by Larry Greenemeier

Much of Intel's success as a microprocessor manufacturer over the past four decades has come from the company's ability to understand and anticipate the future of technology. Intel co-founder Gordon Moore famously asserted in 1965 that the number of transistors that can be placed on an integrated circuit would double every two years. This assessment, which came to be known as Moore's Law, proved to be a highly accurate prediction of what his business could accomplish with generous research and development investments and a meticulous product road map.

As Intel's microprocessors grew smaller, faster and cheaper, they helped to give birth to personal computing and mobile devices that once existed in the realm of science fiction. So it comes as no surprise that science fiction serves as a key inspiration for Brian David Johnson—Intel's official futurist and the man who is paid to craft visions of both Intel's prospective technologies and what coming years hold for the entire computing industry.

One of Johnson's tasks in his unusual role is to promote Intel's Tomorrow Project, launched last year to engage the public in discussions about the direction of computing, as well its impact on society. As part of the Tomorrow Project, Intel also publishes science-fiction anthologies featuring short stories (and including introductions by Johnson) that place emphasis on what hard science portends rather than fantasies

IN BRIEF

WHO
BRIAN DAVID JOHNSON

VOCATION | AVOCATION
Futurist and technology planner

WHERE
Intel Corporation

RESEARCH FOCUS
Future casting—an endeavor that combines computer and social sciences.

BIG PICTURE
In 2020 using a computer won't feel like using a computer at all.

Photograph by Chris Mueller

that break the laws of physics. All these tales, though, are intended to convey the message that humanity ultimately still controls its own destiny.

Scientific American recently spoke with Johnson about what scares people most about the future of technology, what we can learn from the past and what it takes to become a prognosticator (nature or nurture, or a little of both?). Excerpts follow.

Scientific American: What will it will feel like to use a computer in 2020?

JOHNSON: Well, I have good news and bad news. Which do you want first?

Let's start with the bad news, which really isn't bad—it's more pragmatic. In 2020 using a computer will feel remarkably like it does today in 2011. We will still have keyboards and a mouse, touch screens and voice controls. We will still surf the Web and chat with our friends, and many people will still have way too much e-mail in their inbox. I don't think this is a bad thing. I actually find it quite comforting, but it lacks the sizzle of jet packs and rocket cars. Now, let's get to the good stuff.

In 2020 using a computer will be awesome. Just like the mouse, the touch screen and voice [control] radically changed how we interact with computational systems, so, too, will sensor networks, data aggregation and the continuing miniaturization of computational power. I don't really make predictions, but the one thing I can tell you about the future is that we will have more computers and more computational power and that computational power will get further knit into the fabric of our daily lives.

Imagine being able to program your computer just by living with it and by carrying it around with you in your bag. I find this incredibly exciting because it means that how we design and build these systems, how we write the software, how we come up with the cool new apps and great new services, is completely different from how we have in the past 10 years.

Give us an idea of some cool, speculative research that you are following.

I love looking at the parallels between personal computers and synthetic biology [the use of DNA, enzymes and other biological elements to engineer new systems]. Look at how the personal computer grew a little bit out of the counterculture movement, out of the hippie movement, out of the work Intel did and Steve Jobs did and Woz did [Apple cofounder Steve Wozniak]. You see the sort of hacker clubs and small groups of enthusiasts they formed, and you realize what's going on in synthetic biology right now—it's really, really similar. A lot of it is being done by people under the age of 20; a lot of it is being done by enthusiasts who are just getting together and talking about it. Then you can say, if this is true, let's try to judge whether synthetic biology and personal computers are developing at a similar pace. This can help when projecting the future of various technologies.

"The future is completely in motion—it isn't this fixed point out there that we're all sort of running for and can't do anything about."

Have you been doing any actual research on synthetic biology?

I've been doing a lot of work with a synthetic biologist named Andrew Hessel, who collaborates with the Pink Army Cooperative, the folks [promoting individualized therapy for breast cancer]. He's studying the design of viruses, as well as DNA. Think of DNA as the software and an organism—bacterium or virus—as the hardware. You stick the software in, and it actually becomes a computational device.

Consider this, you take a GPS app and put it into your cell phone, and your cell phone becomes a GPS. But what's really awesome about synthetic biology is that you go to sleep with one organism, and when you wake up in the morning there are two, then there are four. They become self-replicating computational devices.

Any ideas?

One fun example that Andrew and I were kicking around was a way to solve "the last mile" for network connectivity. This is literally the last mile between the network hub and your house or apartment. Imagine now that we engineered an organism so that it was an excellent conductor for that Internet signal, better than the cable and copper wires we're using today. Now all we have to do is lay down our little organism between your house and that network hub, and you'll be downloading HD movies day and night.

But how do we do that? Well, what if we crossed our superconducting organism with grass seed so that it looked and grew and could be maintained like grass. Imagine everywhere you see grass that could be a superconducting mesh network that brings the Internet anywhere it grows. And it's alive! Anyone who has ever taken care of a lawn knows that if you treat it right it just keeps growing, sometimes even popping up in places you don't want it. Lawn maintenance and network maintenance become the same thing. That grass median that runs down the middle of many highways across the world could literally become the information superhighway.

How can science fiction influence real-world research and development?

There's a great symbiotic history between science fiction and science fact—fiction informs fact. I do a lot of lectures on AI [artificial intelligence] and robotics, and I talk about inspiration and how we can use science fiction to play around with these ideas. Every time people come to me, pull me aside and say, "You do know the reason why I got into robotics was C3PO, right?" I've become a confessor to some people. I just take their hand and say, "You are not alone. It's okay."

Science fiction inspires people to what they could do. It captures their imagination, which is incredibly important for developing better technology.

How did you become Intel's futurist?

I had been using future casting—a combination of computer science and social science—as part of my work on Intel projects. Before becoming Intel's futurist, I was a consumer experience architect at Intel. This is like a software or silicon architect, except that I designed the entire experience that people would have. A consumer experience architect is part engineer, part designer looking five or 10 years out, toward, for example, the design for system-on-a-chip (SOC) processors, the new type of chip we're putting together with a smaller form factor [meaning smaller dimensions]. Future casting helped us ask ourselves hard questions about the future of technology and figure out what to build. So [Intel's chief technology officer] Justin Rattner said to me, "We think you should be Intel's futurist." And I said, "No way." That's a huge responsibility, especially for a place like Intel.

At the time, Justin wanted me to get out there and start talking to people about the future. We had such discussions internally, but we hadn't been talking about it with others outside the company. The next week [June 30, 2010], we released the book *Screen Future: The Future of Entertainment, Computing and the Devices We Love,* which was about technology in 2015. I sat down and talked to the press. Almost everyone said, "So you're Intel's futurist." At that point, I realized that I already had the job.

How does your role as future caster for Intel fit in with what the company is doing as a maker of microprocessors?

I sit in front of the company's development road map. So I work with a lot of the chip designers in Israel and elsewhere. And every year they remind me that I need to be thinking about, for example, 2020. I create models of what the experience will be like, what it will feel like to use a computer in 2020. Intel is an engineering company, so I turn that into requirements and capabilities for our chips. I'm working on 2019 right now.

How do you ensure that the ideas you have for Intel's future are compatible with the direction that hardware makers (Apple, Dell, and so on), who use Intel chips in their PCs, want to take their products?

The first step in my process is social science. We have ethnographers and anthropologists studying people first and foremost. So all of the future-casting work I do starts with a rich understanding of humans, who are going to use the technology, after all. Then we get into the computer science. Then I do the statistical modeling. Then I start developing models about what the future is going to look like. Then I hit the road.

A huge part of our work is getting out and talking not just to our customers but to the broader ecosystem of government, the military and universities. I ask them, "Where do you see things going? And what will it be like for a person to experience this future?"

Can you give one example about how looking ahead may have helped—or is helping—design an Intel hardware product?

We don't just ask ourselves how can we make the chip smaller and faster and less expensive. Now we ask: What do people need to do with the device? What do we want that final experience to be? What will capture people's imaginations? In *Screen Future,* I wrote about a future where multiple computational devices are connected, all working together so that the consumer won't see any difference between his or her PC or TV or smartphone. For people it will just be about screens: different screens that give us access to the entertainment and the people we love.

Does the act of engaging in imaginative writing help you with your day job?

Writing science fiction has been an integral part of my future-casting process for years. I've used it at Intel to explore the human, cultural and ethical implications of the technologies we're building. Often these stories or science-fiction prototypes are used as a part of the final product specification—this is the requirements document that explains to the engineers and development team what needs to be built. Some of the greatest scientific minds, such as Albert Einstein and Richard Feynman, used creativity and their imagination as a part of their scientific method. When I write science fiction based on science fact, it gives me a really powerful tool to innovate and create technologies that are better designed for humans. Also, engineers love science fiction, so it's a great way to get across my 10- to 15-year future casts.

What is the greatest misconception that people have about the future?

So many people think the future is something that is set. They say, "You're a futurist. Make a prediction." The future is much more complicated than that. The future is completely in motion—it isn't this fixed point out there that we're all sort of running for and can't do anything about. The future is made every day by the actions of people. Because of that, people need to be active participants in that future. The biggest way you can affect the future is to talk about it with your family, your friends, your government. SA

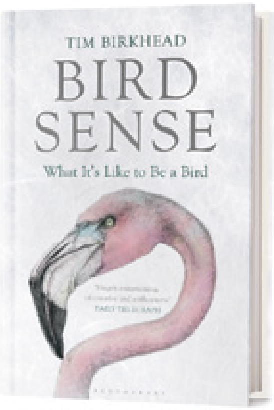
Larry Greenemeier *is an associate editor at* Scientific American.

MORE TO EXPLORE

The Tomorrow Project Anthology: Conversations about the Future. Cory Doctorow, will.i.am, Douglas Rushkoff and Brian David Johnson. Intel Corporation, 2011.

SCIENTIFIC AMERICAN ONLINE
Read more questions with Johnson at ScientificAmerican/may2012/intel-futurist

BOOKS

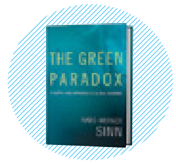


> *"The sensory biology of birds is about to have its day."* —*From* Bird Sense

Bird Sense: What It's Like to Be a Bird

by Tim Birkhead. Walker & Company, 2012 ($25)

Birds are more like humans than many realize: they are bipedal, they rely primarily on sight and hearing, and most are monogamous. Birkhead, a professor at the University of Sheffield in England, has spent his career studying bird behavior and fills his book with evocative stories and observations about numerous species, including flamingos, parrots and his beloved long-tailed sylph hummingbird. Each chapter is devoted to a particular sense or trait—"Touch," "Hearing," "Seeing"—with "Emotions" being one of the most nuanced. Birds perform increasingly elaborate greeting rituals the longer they have been away from their partner, he writes. Does that mean they experience feelings the same way humans do? Birkhead is reluctant to draw a conclusion, letting the observations speak for themselves.



The Green Paradox: A Supply-Side Approach to Global Warming

by Hans-Werner Sinn. MIT Press, 2012 ($29.95)

This English translation of a European best seller lays out German economist Sinn's controversial ideas about how to reduce carbon emissions. European and American politicians, he argues, are too focused on reducing fossil-fuel demand and not focused enough on curbing supply. As a solution, he proposes a "Super-Kyoto" scheme in which consumer countries would form a cap-and-trade system that would limit each government's fossil-fuel purchases—similar to the way ration cards worked during World War II. In addition, the cartel would levy source taxes on producers' capital income, encouraging them to leave more of their resources underground.

DNA USA: A Genetic Portrait of America

by Bryan Sykes. Liveright, 2012 ($27.95)

University of Oxford geneticist Sykes sets off on a three-month journey across the U.S., accompanied for a time by his teenage son, who is about to go off to college, collecting spit from volunteers along the way. The result is a beautifully written travelogue and valuable genetics primer that paints an intriguing, anthropological history of the country. Some of Sykes's (not always surprising) results suggest that racial intermixing appears least common in New England, that nearly all Americans whose ancestors arrived as slaves from Africa have European DNA, and that European genes began mixing with those of Native Americans some 10,000 years ago, hinting at a possible European origin for some Native Americans.

Floating Gold: A Natural (and Unnatural) History of Ambergris

by Christopher Kemp. University of Chicago Press, 2012 ($22.50)

Kemp has hit on a fascinating yet almost entirely unknown subject: ambergris, a rare by-product of sperm whale digestion that is worth nearly as much as gold. Its value comes primarily from its scarcity: an estimated 1 percent of sperm whales produce it, and circumstances have to be just right for it to wash up on shore. Whereas ambergris is usually fatal to the whales that produce it (it can rupture their intestines, as described in one grim passage), it has been prized by perfume houses for its stabilizing effect and "animalic" scent and by collectors who use it as an aphrodisiac. Kemp's perseverance in unraveling this story is admirable, although the book's pacing is uneven.

MULTIMEDIA

Catlin Seaview Survey. Visitors to this Web site can examine sections of Australia's Great Barrier Reef (*below*) using the survey's new 360-degree underwater viewer: **www.catlin-seaviewsurvey.com/seaview.htm**

High Seas Adventures. This feature from the British Library's 19th Century Historical Collection iPad app offers more than 100 works of nautical literature covering Arctic expeditions, shipwrecks, pirate attacks, and more.

Deep Sea News. An informative blog about the oceans written largely by marine biologists. **http://deepseanews.com**

SEA VIEW: Humphead wrasse

COURTESY OF CATLIN SEAVIEW SURVEY

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

Much Ado about Nothing

Science closes in on why there is something instead of nothing

Why is there something rather than nothing? This is one of those profound questions that is easy to ask but difficult to answer. For millennia humans simply said, "God did it": a creator existed before the universe and brought it into existence out of nothing. But this just begs the question of what created God—and if God does not need a creator, logic dictates that neither does the universe. Science deals with natural (not supernatural) causes and, as such, has several ways of exploring where the "something" came from.

Multiple universes. There are many multiverse hypotheses predicted from mathematics and physics that show how our universe may have been born from another universe. For example, our universe may be just one of many bubble universes with varying laws of nature. Those universes with laws similar to ours will produce stars, some of which collapse into black holes and singularities that give birth to new universes—in a manner similar to the singularity that physicists believe gave rise to the big bang.

M-theory. In his and Leonard Mlodinow's 2010 book, *The Grand Design,* Stephen Hawking embraces "M-theory" (an extension of string theory that includes 11 dimensions) as "the only candidate for a complete theory of the universe. If it is finite—and this has yet to be proved—it will be a model of a universe that creates itself."

Quantum foam creation. The "nothing" of the vacuum of space actually consists of subatomic spacetime turbulence at extremely small distances measurable at the Planck scale—the length at which the structure of spacetime is dominated by quantum gravity. At this scale, the Heisenberg uncertainty principle allows energy to briefly decay into particles and antiparticles, thereby producing "something" from "nothing."

Nothing is unstable. In his new book, *A Universe from Nothing,* cosmologist Lawrence M. Krauss attempts to link quantum physics to Einstein's general theory of relativity to explain the origin of a universe from nothing: "In quantum gravity, universes can, and indeed always will, spontaneously appear from nothing. Such universes need not be empty, but can have matter and radiation in them, as long as the total energy, including the negative energy associated with gravity [balancing the positive energy of matter], is zero." Furthermore, "for the closed universes that might be created through such mechanisms to last for longer than infinitesimal times, something like inflation is necessary." Observations show that the universe is in fact flat (there is just enough matter to slow its expansion but not to halt it), has zero total energy and underwent rapid inflation, or expansion, soon after the big bang, as described by inflationary cosmology. Krauss concludes: "Quantum gravity not only appears to allow universes to be created from nothing—meaning ... absence of space and time—it may require them. 'Nothing'—in this case no space, no time, no anything!—is unstable."

The other hypotheses are also testable. The idea that new universes can emerge from collapsing black holes may be illuminated through additional knowledge about the properties of black holes, which are being studied now. Other bubble universes might be detected in the subtle temperature variations of the cosmic microwave background radiation left over from the big bang of our own universe. NASA's Wilkinson Microwave Anisotropy Probe (WMAP) spacecraft is collecting data on this radiation. Additionally, the Laser Interferometer Gravitational Wave Observatory (LIGO) is designed to detect exceptionally faint gravitational waves. If there are other universes, perhaps ripples in gravitational waves will signal their presence. Maybe gravity is such a relatively weak force (compared with electromagnetism and the nuclear forces) because some of it "leaks" out to other universes.

Even if God is hypothesized as the creator of the laws of nature that caused the universe (or multiverse) to pop into existence out of nothing—if such laws are deterministic—then God had no choice in the creation of the universe and thus was not needed. In any case, why turn to the supernatural when our understanding of the natural is still in its incipient stages? We would be wise to heed this skeptical principle: before you say something is out of this world, first make sure that it is not in this world. SA

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/may2012

Illustration by Neil Webb

SCIENTIFIC AMERICAN™ Travel BRIGHT HORIZONS™ 15

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Face the challenges posed by conservation planning and wildfire management, guided by Dr. Yohay Carmel. Dive into discoveries in astro-particle physics with Dr. David Lunney. Glimpse the neuroscience behind sensory perception and visual illusions with Dr. Stephen Macnik and Dr. Susana Martinez-Conde. Focus on developments in the nature and maintenance of memory with Dr. Jeanette Norden. Take in evolving thought on humankind's emigration from Africa with Professor Chris Stringer.

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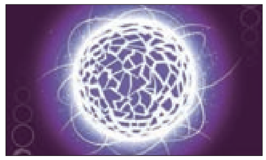


NUCLEAR ASTROPHYSICS

Speaker: David Lunney, Ph.D.

A Hitchhiker's Guide to the Universe

An introduction to the formation and composition of the visible universe, emphasizing the synthesis of Earth's chemical elements in the stars. Discover the key reactions, the evolutionary process of nuclear systems, and the forces that shape ongoing debates in nuclear astrophysics.

Nuclear Cooking Class

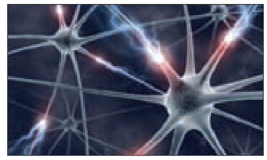
Get cooking with a discussion of the physics behind element formation by fusion and capture reactions. Dr. Lunney will highlight the need to weigh ingredient atoms to precisely determine mass. Take a seat in a precise corner of the physics kitchen and feast on the latest on nucleosynthesis.

Weighing Single Atoms

The most precise balance known to man is an electromagnetic trap in which ionized atoms are made to dance, revealing their mass. We'll look at the basics of atomic mass measurement. Learn about current techniques of mass measurement, how these methods compare, and the diverse programs worldwide that use them. Glimpse the shape of the future of precision measurement.

Panning the Seafloor for Plutonium: Attack of the Deathstar

Long, long ago, not so far away, did an exploding supernova bathe our planet with its stellar innards? Explore the research, theories, and phenomena that suggest the role of a local supernova in the creation of the sun and its planetary system.



NEUROSCIENCE MEMORY

Speaker: Jeanette Norden, Ph.D.

How the Brain Works

Get the lay of the land in this introductory neuroscience session showing how the brain is divided into functional systems. A special emphasis will be on limbic and reticular systems, which underlie learning and memory, executive function, arousal, attention, and consciousness.

Memory and All That Jazz

Memory is among the most precious of human abilities. Find out what neuroscience has revealed about how we learn and remember. Pinpoint how different areas of the brain encode different types of information—from the phone number we need to remember for only a moment to the childhood memories we retain for a lifetime.

Losing your Memory

When we lose our memories, we lose a critical part of ourselves and our lives. Dr. Norden will introduce the many clinical conditions that can affect different types of learning and memory.

Use it or Lose it!

While memory can be lost under a wide variety of clinical conditions, most memory loss during aging is not due to strokes or neurodegenerative disease, but to lifestyle. Building evidence suggests that aging need not lead to significant memory loss. Find out how to keep your brain healthy as you age.

COGNITIVE NEUROSCIENCE

Speakers: Stephen Macknik, Ph.D. and Susana Martinez-Conde, Ph.D.

How the Brain Constructs the World We See

All understanding of life experiences is derived from brain processes, not necessarily the result of actual events. Neuroscientists are researching the cerebral processes underlying perception to understand our experience of the universe. Discover how the brain constructs, not reconstructs, the world we see.

Cognitive Neuroscience, cont.

Windows on the Mind

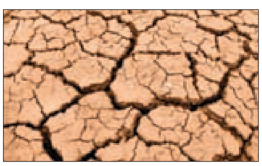
What's the connection behind eye movements and subliminal thought? Join Dr. Macknik and Dr. Martinez-Conde in a look at the latest neurobiology behind microsaccades, the involuntary eye movements that relate to perception and cognition. Learn how microsaccades suggest bias toward certain objects, their relationship to visual illusions, and the pressing questions spurring visual neurophysiologists onward.

Champions of Illusion

The study of visual illusions is critical to understanding the basic mechanisms of sensory perception and advancing cures for visual and neurological diseases. Connoisseurs of illusion, Dr. Macknik and Dr. Martinez-Conde produce the annual Best Illusion of the Year Contest. Study the most exciting novel illusions with them and learn what makes these brain tricks work.

Sleights of Mind

Magic fools us because humans have hardwired processes of attention and awareness that can be "hacked." A good magician employs the mind's own intrinsic properties. Magicians' insights, gained over centuries of informal experimentation, have led to new discoveries in the cognitive sciences, and reveal how our brains work in everyday situations. Get a front-row seat as the key connections between magic and the mind are unveiled!



CLIMATOLOGY

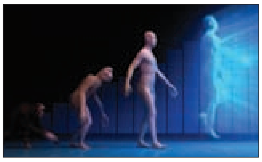
Speaker: Yohay Carmel, Ph.D.

Prioritizing Land for Nature Conservation: Theory and Practice

Forest clearing, climate change, and urban sprawl are transforming our planet at an accelerating rate. Conservation planning prescribes principles and practical solutions for selecting land for protection, assigning land for development, and minimizing the negative impact on nature. Taking a bird's-eye view of approaches to conservation, we'll put the hot topics and tough questions in perspective through an insightful discussion.

Facing a New Mega-Fire Reality

Worldwide, the area, number, and intensity of wildland fires has grown significantly in the past decade. Fire-protection strategies used in the past may not work in the future. Learn the roots and causes of wildfires and recent efforts to predict, manage, and mitigate fire risk. Gain food for thought about the complex interface between science and policy.



HUMAN EVOLUTION

Speaker: Chris Stringer, Ph.D.

Human Evolution: the Big Picture

Time-travel through 6 million years of human evolution, from the divergence from African apes to the emergence of humans. In 1871, Charles Darwin suggested that human evolution had begun in Africa. Learn how Darwin's ideas stand up to the latest discoveries, putting his tenets into context and perspective.

The First Humans

About 2 million years ago the first humans appeared in Africa, distinctly different from their more ancient African ancestors. Discover what drove their evolution and led to a spread from their evolutionary homeland to Asia and Europe. Explore current thinking on the early stages of human evolution.

The Neanderthals: Another Kind of Human

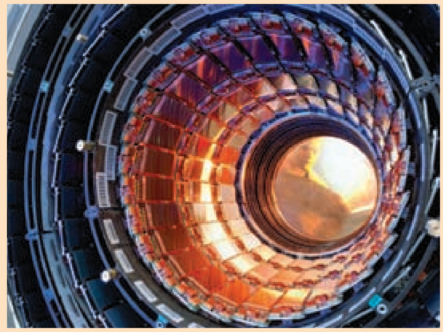
Our close relatives, the Neanderthals, evolved in parallel with *Homo sapiens*. Often depicted as bestial ape-men, in reality they walked upright as well as we do, and their brains were as large as ours. So how much like us were they? What was their fate? Track the evolution of the Neanderthals in light of the latest discoveries.

The Rise of *Homo Sapiens*

Modern humans are characterized by large brains and creativity. How did our species arise and spread across the world? How did we interact with other human species? We will examine theories about modern human origins, including Recent African Origin ("Out of Africa"), Assimilation, and Multiregional Evolution, and delve in to the origins of human behavioral traits.

SCIENTIFIC AMERICAN Travel HIGHLIGHTS

INSIDER'S TOUR OF CERN



Pre-cruise: October 22, 2012—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 full-day tour of this iconic nuclear-research facility.

Whether you lean toward concept or application, there's much to pique your curiosity. Discover the excitement of fundamental research and get an insider's look at the world's largest particle physics laboratory.

Our full-day tour will be led by a CERN physicist. We'll have an orientation, visit an accelerator and experiment, get a sense of the mechanics of the Large Hadron Collider (LHC), make a refueling stop for lunch, and have time to peruse exhibits and media on the history of CERN and the nature of its work.

This tour includes: Bus transfer from Geneva, Switzerland to our Genoa, Italy hotel (October 23) • 3 nights' hotel (October 20, 21, 22) • 3 full breakfasts (October 21, 22, 23) • Transfers to and from the hotel on tour day (October 22) • Lunch at CERN • Cocktail party following our CERN visit • Do-as-you-please day in Geneva, including transfers to and from downtown (October 21) • Transfer from airport to our Geneva hotel

The price is $899 per person (based on double occupancy). This trip is limited to 50 people. NOTE: CERN charges no entrance fee to visitors.

EPHESUS

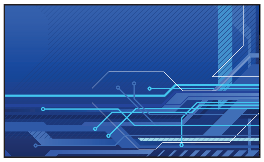
November 1, 2012—Many civilizations have left their mark at Ephesus. It's a complex and many-splendored history, often oversimplified. Bright Horizons pulls together three important aspects of understanding Ephesus that are rarely presented together. You'll meander the Marble Road, visit the legendary latrines, check out the Library, and visit the political and commercial centers of the city. A visit to the Terrace Houses will enhance your picture of Roman-era Ephesus.

We'll take a break for Mediterranean cuisine in the Selcuk countryside, then visit the Ephesus Museum in Selcuk, where city excavation finds are showcased, and you'll get a fuller look at local history, from the Lydians to the Byzantines.

ATHENS

November 1, 2012—The Parthenon and its Acropolis setting are stunning, no doubt about it. Requiring no interpretation, they are ideal for a DIY Athens excursion. On the other hand, visiting the new Acropolis Museum and the National Archaeological Museum with a skilled guide who's on your wavelength adds immeasurably to the experience. We suggest you join Bright Horizons on a focused trip. You'll see the Parthenon frieze, exquisite sanctuary relics, and Archaic sculpture at the Acropolis Museum (as you can see from the picture, the museum sits just below the Acropolis).

Lunch is tucked away at a taverna favored by Athenian families. For dessert, we'll visit the richest array of Greek antiquities anywhere—at the National Archaeological Museum.



NANOSCIENCE

Chris Sorensen, Ph.D.

Fire, Fractals and the Divine Proportion

Physicist Chris Sorenson discusses the mysteries, beauties, and curiosities of soot. Take an unlikely journey of discovery of soot to find fractal structures with non-Euclidian dimensionality, networks that tenuously span space and commonalities among spirals, sunflowers and soot. Gain an appreciation for the unity of Nature, and the profound lessons in the commonplace as well as the sublime through soot!

Light Scattering

Take a *particle* physics perspective and ask: how do particles scatter light and why does light scatter in the first place? What are the effects of scattering on the polarization? How do rainbows, glories and sundogs work? How do light scattering and absorption effect the environment? Get the latest on scattering and see your universe in a new light.

Nanoparticles: The Technology.

Nanoscience has spawned a significant nanotechnology. Explore new nanomaterials such as self cleaning surfaces and fibers stronger yet lighter than steel. Then we'll do some informed daydreaming about far reaching possibilities like nanobots that could take a "fantastic voyage" inside your body or stealth materials for the invisible man. Enjoy reality science fiction at its best!

Nanoparticles: The Science.

What makes "nano" so special? Why does nano hold such great promise? Take a look at the clever chemistry that creates the nanoparticle building blocks of the new nanomaterials. Find out why physical properties of nanoparticles differ from larger particles. When this session is over, you'll understand why small can be better.

ASTROBIOLOGY

Speaker: Seth Shostak, Ph.D.

Hunting for Life Beyond Earth

Is Earth the only planet to sport life? Researchers are hot on the trail of biology beyond Earth, and there's good reason to think that we might find it within a decade or two. How will we find alien biology, and what would it mean to learn that life is not a miracle, but as common as cheap motels?

Finding E.T.

Life might be commonplace, but what about intelligent life? What's being done to find our cosmic confreres, and what are the chances we'll discover them soon? While most people expect that the cosmos is populated with anthropomorphic aliens aka "little gray guys with large eyes and no hair" you'll hear that the truth could be enormously different.

What Happens If We Find the Aliens?

One-third of the public believes that aliens are visiting Earth, pirouetting across the skies in their saucers. Few scientists agree, but researchers may soon discover intelligent beings sharing our part of the galaxy. Could we handle the news? What facts could be gleaned

immediately, and what would be the long-term effects such a discovery would have on us and our institutions, such as religion?

The Entire History of the Universe

Where and when did the cosmos begin, and what's our deep, deep future? The book of Genesis gives only a short description of the birth of the cosmos, but modern science can tell a more complex tale. How did the universe get started, and could there be other universes? And how does it all end, or does it end at all?

SKEPTICISM

Speaker: Michael Shermer, Ph.D.

The Believing Brain: From Ghosts and Gods to Politics and Conspiracies — How We Construct Beliefs and Reinforce Them as Truths

The brain as a "belief engine"? Learn how our brains' pattern-recognition and confirmation bias help form and reinforce beliefs. Dr. Shermer provides real-world examples of the process from politics, economics, and religion to conspiracy theories, the supernatural, and the paranormal. This discussion will leave you confident that science is the best tool to determine whether beliefs match reality.

Skepticism 101: How to Think Like a Scientist

Harvest decades of insights for skeptical thinking and brush up on critical analysis skills in a lively session that addresses the most mysterious, controversial, and contentious issues in science and skepticism. Learn how to think scientifically and skeptically. You'll see how to be open-minded enough to accept new ideas without being *too* open-minded.

The Science of Good and Evil: The Origins of Morality and How to be Good Without God

Tackle two challenging questions of our age with Michael Shermer: (1) The origins of morality and (2) the foundations of ethics. Dr. Shermer peels back the inner layers covering our core being to reveal complex human motives — good and evil. Gain an understanding of the evolutionary and cultural underpinnings of morality and ethics and how these motives came into being.

The Mind of the Market: Compassionate Apes, Competitive Humans, and Other Lessons from Evolutionary Economics

How did we evolve from ancient hunter-gatherers to modern consumer-traders? Why are people so irrational when it comes to money and business? Michael Shermer argues that evolution provides an answer to both of these questions through the new science of evolutionary economics. Learn how evolution and economics are both examples of complex adaptive systems. Get your evolutionary economics tools together.

SCIENTIFIC AMERICAN Travel HIGHLIGHTS

IGUAZU FALLS

March 5–7, 2013 — Surround yourself with 260 degrees of 240 foot-high walls of water at Iguazu Falls. Straddling the Argentinian-Brazilian border, Iguazu Falls is split into about 270 discrete falls and at peak flow has a surface area of 1.3 million square feet. (By comparison, Niagara Falls has a surface area of under 600,000 square feet.) Iguazu is famous for its panoramic views and breath-taking vistas of huge sprays of water, lush rainforest, and diverse wildlife.

You'll walk Iguazu National Park's extensive and well-engineered circuit paths over the Falls, go on a boat ride under the Falls, be bowled over by the massiveness and eco-beauty, and take a bazillion pictures.

MACHU PICCHU

February 15–20, 2013 — Scale the Andes and absorb Machu Picchu's aura. Visit this legendary site of the Inca World, draped over the Eastern slopes of the Peruvian, wrapped in mystery. Whether it was an estate for the Inca emperor Pachacuti or a site for astronomical calculations, it captures the imagination. Visit Machu Picchu, and see for yourself the massive polished dry-stone structures, the Intihuatana ("Hitching Post of the Sun"), the Temple of the Sun, and the Room of the Three Windows. Iconic ruins, rich flora and fauna, and incomparable views await your eye (and your lens).

EASTER ISLAND

Febrruary 16–20, 2013 — The moai of Easter Island linger in many a mind's eye, monumental statues gazing inland, away from the South Pacific. Join Bright Horizons on a four-day pre-cruise excursion to explore the mysteries of Rapa Nui. Visit archaeological sites, learn about the complex cultural and natural history of the island, and absorb the ambiance of one of the most remote communities on Earth. Come along on an adventure where archaeology and environment create memories and food for thought.

GALAPAGOS

February 12–20, 2013 — Enter an unearthly natural world in an eight-day pre-cruise excursion to the Galapagos Islands. "See the world in a grain of sand" and hone your knowledge of evolution with your observations in the Galapagos, a self-contained natural history laboratory. We'll tour Santiago, Chile, and straddle the Equator at the "Middle of the World" complex in Quito, Ecuador. Then off to the Galapagos for a four-day expedition on the mv Galapagos Legend. Accompanied by certified naturalists see the incredibly diverse flora and fauna up close. You'll have the opportunity to swim and snorkel, and photograph legendary wildlife and wild landscapes. Join Bright Horizons in the Galapagos for all the intangibles that communing with nature provides.

The ongoing search for fundamental farces

Steve Mirsky has been writing the Anti Gravity column since a typical tectonic plate was about 33 inches from its current location. He also hosts the *Scientific American* podcast Science Talk.

Math Rules

Some equations touch all our lives—while others, well, not so much

In his new book, *In Pursuit of the Unknown: 17 Equations That Changed the World,* Ian Stewart recounts one of the worst jokes in the history of science. You can develop your own setup from first principles once you know the punch line: "The squaw on the hippopotamus is equal to the sum of the squaws on the other two hides." Never mind how Native Americans were in possession of a hippopotamus—the important thing is that the Pythagorean theorem is so well known that comedy writers consider it fair game even if that game couldn't possibly be found on the correct continent.

Stewart, who formerly wrote the Mathematical Recreations column for *Scientific American,* takes the reader on an engaging tour of vital math for a modern world. We go from Pythagoras' right triangle ($a^2 + b^2 = c^2$)—nice—to Newton's law of gravity ($F = G\frac{m_1 m_2}{r_2}$)—good—to Einstein's special theory of relativity ($E = mc^2$)—still with you—to the Navier-Stokes equation governing the movement of fluids—$\rho(\frac{\partial v}{\partial t} + v \cdot \nabla v) = -\nabla p + \nabla \cdot T + f$—which pretty much convinced me to change my career trajectory from science to science journalism.

I highly recommend Stewart's wonderfully accessible book and now share with you some additional equations not in its pages but of importance to me, personally.

$HA > H$ AT ANY TIME (t)

Technically an inequality, $HA > H(t)$ means that at any time (t), the number of horses' asses (HA) will exceed the number of horses (H). (Time should be understood to be limited to the period starting with the evolution of modern humans and ending with our eventual extinction.)

This concept is so obvious as to practically have the standing of axiomatic truth. The inequality clearly holds at racetracks and equestrian events, where HA may only slightly outnumber H. (Have you seen the hats some of those horsey folk wear?) Its true power to describe reality, however, is on display in situations where H may vanish to 0, such as professional wrestling or the vast majority of the programming on C-Span.

$P_{SM}(L) = 0$

Someone's winning the lottery, but not me.

$M_{S1 + S2} + 3_d = WTS$

I discovered this equation only in the past few months, when I was traveling and working odd hours to the point of abandoning customary daily ablutions. The equation states that three days (3_d) after your last shower ($S1$) and shave ($S2$), any man (M) will look exactly like William Tecumseh Sherman.

$20x + 10y + 5z = 0_C$

This equation clearly states that when attempting to use a vending machine that takes singles, you will have in your possession some integer numbers of 20s, 10s and fives but no ones—and, therefore, no candy.

$$OPS = \frac{AB \times (H + BB + HBP) + TB \times (AB + BB + SF + HBP)}{AB \times (AB + BB + SF + HBP)}$$

When I was 10 years old, I started devoting ridiculous amounts of time to the analysis and generation of baseball statistics. Back then, it only got about as complicated as batting average equaling hits divided by at bats. Now, thanks to Bill James and other mathematically oriented fans, we have much more valuable stats, such as on base plus slugging (OPS), which also stands for the reaction of more casual fans to one's spouting about it—namely, "Oh, please, shuddup."

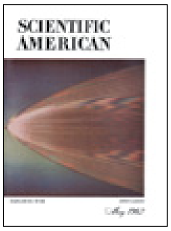
$0.5X = 100$

This equation had a major effect on a friend, which cascaded in my direction. The friend wanted to be an automotive engineer. But he had performed poorly in high school algebra and knew that there was more complex math to come on the way to any engineering career. So we worked for many hours on the algebraic basics. At the end of said hours, my friend was able to determine that 0.5×100 was equal to 50. But the leap to determining the X in $0.5X = 100$ remained unleapt, which led to my advice that he consider a career as rewarding as automotive engineering that avoided complicated figuring. He went on to become an automobile insurance adjuster and is an invaluable resource to me whenever my car is struck by some HA. SA

SCIENTIFIC AMERICAN ONLINE
Comment on this article at ScientificAmerican.com/may2012

Illustration by Matt Collins

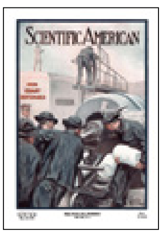
Innovation and discovery as chronicled in *Scientific American*



May 1962

First Gamma-Ray Satellite

"Within the past year or so the merest glimpse has been obtained of the universe as revealed by the very-high-energy photons called gamma rays. The glimpse has been provided by fewer than 100 energetic photons, recorded by a gamma ray 'telescope' carried into orbit on April 27, 1961, by the artificial satellite Explorer XI. It is doubtful whether such a small number of particles have ever before been analyzed so intensively in an effort to extract information about the universe. The analysis is still continuing in our laboratory at the Massachusetts Institute of Technology, and the entire sample of events that we are prepared to discuss numbers only 22. —William L. Kraushaar and George W. Clark"



May 1912

Montessori Method

"It is not yet clear to what the great popular interest in Dr. Maria Montessori's method is due. Is it the fact that we are all so much dissatisfied with the results of our educational efforts that we look with interest to every new method offered; or is it that we now have means for securing publicity that were not available to educational reformers of earlier times? Whatever the cause, the interest is well deserved. Here is a woman, scientifically trained, with a broad love of humanity and high educational ideals, who has devoted years of her life to developing what she considers a rational and effective method of educating children between the ages of three and six. She uses, to a great extent, methods that have been successful in the training of defectives. Applying them to normal children, her results have been truly remarkable."

Retail Theory

"There are as many women as there are men who pursue odd ways of earning money, one class of which would be designated as 'goats,' for it is their business to be 'discharged' from the department stores in which they are 'employed' a number of times each day. When a grouchy or haughty customer makes complaint of discourteous treatment against a clerk, one of the 'goats' is summoned to the office as the person in charge of that particular department. There she is given a good talking to in front of the angry customer and summarily 'dismissed,' and the complainant goes away rejoicing."


Scientific American.

May 1862

Underground Railway

"A subterranean railway in London is now in an advanced state of construction, running about four and a half miles under the city of London. It commences at Victoria Street, in the midst of what was formerly a disreputable thoroughfare, but is now a common center for the Great Northern, the London, Chatham and Dover, and the Metropolitan lines. On the occasion of a recent trip made through a portion of its length, the air was found to be perfectly sweet, and free from all unpleasantness or dampness. The locomotives used condense their steam and consume their own smoke, so that neither gas nor vapor is perceptible."

The railway opened in 1863; portions of its tunnels are still used in the modern London Underground.

Sled Invention

"Every boy may now slide down the steep sides of snow-covered hills sitting comfortably in an upright position, legs and feet all aboard, guiding his vehicle by reins, as if he were driving a mettled steed. It will be seen by glancing at the engraving how this is accomplished by a new invention, Isaac N. Brown's coasting sled, which has a guiding runner attached to the front of the sled. The engraving also illustrates the danger of sliding the old kind, such as we used when a boy."

This sled seems like such a great idea—and who can ignore the cautionary tale in the drawing? For other great ideas from 1862, some workable, some not, see the slideshow at www.ScientificAmerican.com/may2012/inventions

STEERABLE SLED: Brown's coasting sled from 1862, for when the weather is cold and snowy—and the sorry fate of the unfortunate child who does not have one.

SCIENTIFIC AMERICAN, VOL. VI, NO. 19; MAY 10, 1862

High and Dry in the Food Desert

Where fresh foods are scarce, so is good health

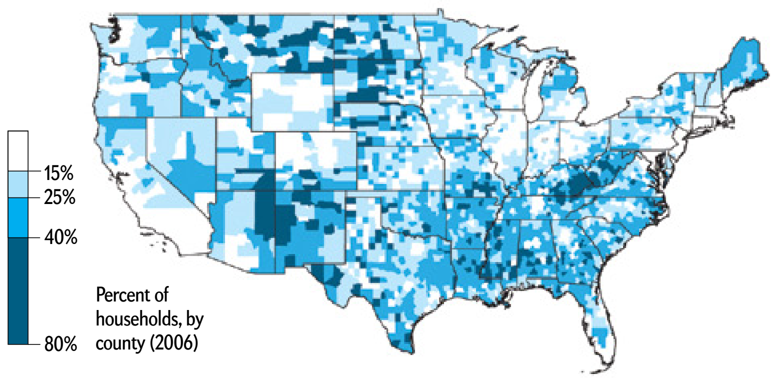
Even within the borders of one of the world's top agricultural countries, healthy food can be hard to come by. Many Americans reside in food deserts—communities where retailers offering fresh food are scarce but fast-food restaurants and convenience stores selling prepared foods can abound.

The top two maps at the right show the proximity of full-line grocers to two groups for whom healthy food is often difficult to procure: low-income households and those without access to a vehicle. Scientists are still exploring the links between food deserts and health by investigating how the nonavailability of fresh food may spur obesity, diabetes and other diet-related conditions. One 2006 study found an association between the presence of supermarkets and lower obesity rates. Convenience stores, on the other hand, were associated with higher rates.

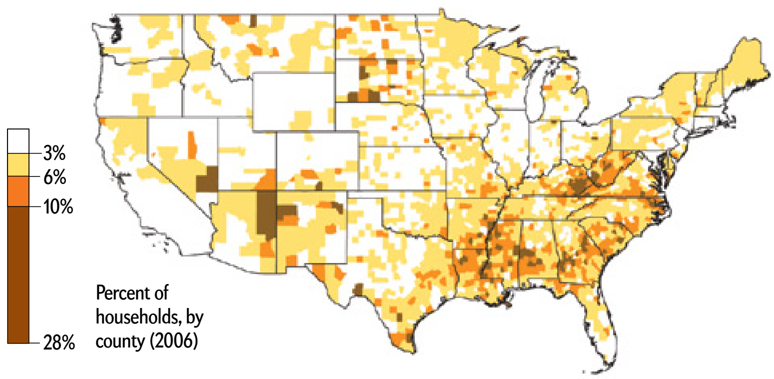
"You always have to be careful about suggesting cause and effect," says Mari Gallagher, whose Chicago consulting firm carries out case studies of local food environments. The relation between food and health is complex, and personal choice clearly plays a role. "But we do think that the environment, in a lot of different ways, matters," Gallagher says. "You can't choose healthy food if you don't have access to it." *—John Matson*

SCIENTIFIC AMERICAN ONLINE
More maps of food deserts at ScientificAmerican.com/may2012/graphic-science

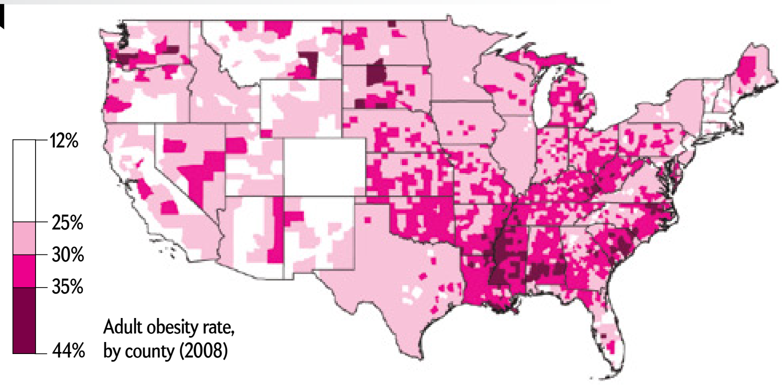
Low-Income Households (more than 1 mile from a grocery)



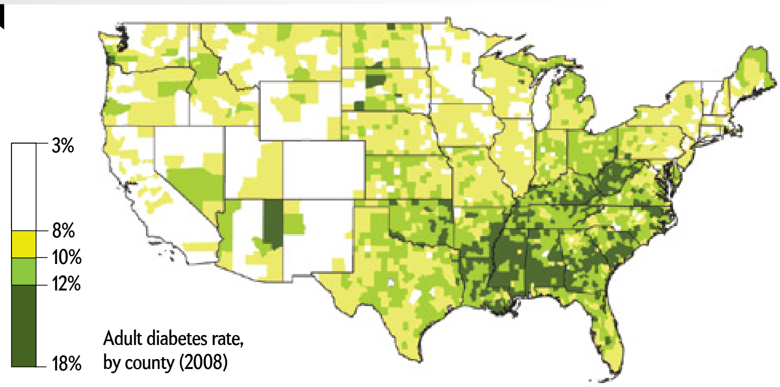
Car-Free Households (more than 1 mile from a grocery)



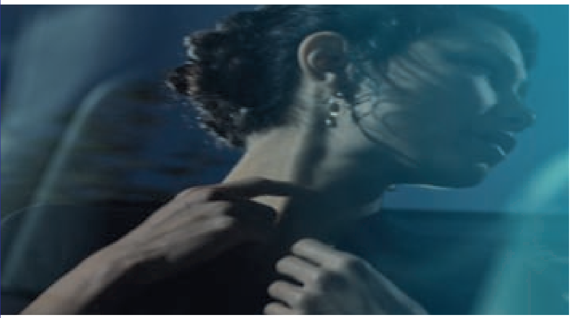
Health Indicator: Obesity



Health Indicator: Diabetes



SOURCE: *FOOD ENVIRONMENT ATLAS*, U.S. DEPARTMENT OF AGRICULTURE, ECONOMIC RESEARCH SERVICE



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