Medicine
How to Find the Best Treatments

Climate Science
The Last Great Global Warming

Electronics
Hacking the Power Grid

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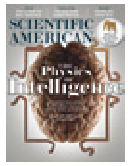
SCIENTIFIC AMERICAN

July 2011 Volume 305, Number 1

ON THE COVER



Various lines of research suggest that most conceivable ways of improving brainpower would face fundamental limits similar to those that affect computer chips. Has evolution made us nearly as smart as the laws of physics will allow? Brain photographed by Adam Voorhes at the Department of Psychology, Institute for Neuroscience, University of Texas at Austin. Graphic element by 2FAKE.

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FEATURES

Photograph by Floto + Warner


NORTHROP GRUMMAN
What if we could detect planets that are able to sustain life?
What if we could glimpse the Universe in its infancy?
What if we could stop asking "What if?"
www.northropgrumman.com/webbtelescope
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Photo courtesy of NASA, ESA, M. Robberto, and the Hubble Space Telescope Orion Treasury Project Team.


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SCIENTIFIC AMERICAN

DEPARTMENTS

ON THE WEB

The Science of Fatherhood
Just in time for Father's Day, Scientific American takes a look at research into the paternal bond and how evolution and modern society combine to shape the experience of fatherhood.
Go to www.ScientificAmerican.com/jul2011/fathers

RICHARD PRICE *Getty Images (cornfield);* TAYLOR LOCKWOOD *(tropical oyster mushroom)*

Scientific American (ISSN 0036-8733), Volume 305, Number 1, July 2011, published monthly by Scientific American, a division of Nature America, Inc., 75 Varick Street, 9th Floor, New York, N.Y. 10013-1917. Periodicals postage paid at New York, N.Y., and at additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; QST No. Q1015332537. Publication Mail Agreement #40012504. Return undeliverable mail to Scientific American, P.O. Box 819, Stn Main, Markham, ON L3P 8A2. **Individual Subscription rates:** 1 year $39.97 (USD), Canada $49.97 (USD), International $61 (USD). **Institutional Subscription rates:** Schools and Public Libraries: 1 year $69 (USD), Canada $74 (USD), International $81 (USD). Businesses and Colleges/Universities: 1 year $299 (USD), Canada $304 (USD), International $311 (USD). Postmaster: Send address changes to Scientific American, Box 3187, Harlan, Iowa 51537. **Reprints available:** write Reprint Department, Scientific American, 75 Varick Street, 9th Floor, New York, N.Y. 10013-1917; fax: 646-563-7138; reprints@SciAm.com. **Subscription inquiries: U.S. and Canada (800) 333-1199; other (515) 248-7684. Send e-mail to sacust@sciam.com.** Printed in U.S.A.

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

Honors and Activities

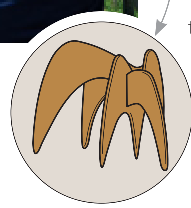
Magician David Copperfield waved his hand over the envelope, which popped open. He wiggled his fingers, and the card slid upward. A moment later we heard the winner's name: "*Scientific American*." The guests at our tables roared with approval.

A group of *Scientific American* colleagues were at the 2011 National Magazine Awards, the Oscars of publishing. The magazine won for General Excellence in the category of "Finance, Technology and Lifestyle Magazines." The award, bestowed by the American Society of Magazine Editors, was for the September, November and December 2010 issues.

The staff worked hard, but we owe special thanks to our readers. You inspire and challenge the editors, art directors and others with your insights, observations, feedback and suggestions. You have high expectations, and we aim to meet them.

In this month's cover story, for instance, "The Limits of Intelligence," author Douglas Fox explains how the laws of physics may well prevent the human brain from evolving into an ever more powerful thinking machine. Turn to page 36 to find out why. Other articles in the issue explore how experts can identify "The *Best* Medicine" via comparative effectiveness research (*page 50*); what lessons "The Last Great Global Warming" 56 million years ago offers today (*page 56*); and how confounding the "Scent of a Human" for mosquitoes could combat malaria (*page 76*). Rounding out the mix is a feature marking the 100th anniversary of "The Periodic Table of the Cosmos," which reveals the patterns behind the stellar bestiary (*page 44*).

Building a bunny-coptor with a friend and the Lawrence Hall of Science crew.



The Ellie, bestowed by the American Society of Magazine Editors at the National Magazine Awards in New York City.

Last, I want to mention two items. First, thanks to the Lawrence Hall of Science in Berkeley, Calif., for inviting me to join them at the White House Easter Egg Roll, which began including family-friendly science activities last year. We built bunny-shaped copters and kites with the kids. Check out *Scientific American*'s educational activities at www.ScientificAmerican.com/education.

Second, in July the Google Science Fair will announce its first contest winners, which invited entries from students ages 13 to 18. I will be the chief judge and master of ceremonies. Watch us on YouTube and learn more at www.google.com/sciencefair. SA

COURTESY OF CHRISTINE RUFFO *Association of Science-Technology Centers*

Illustration by Nick Higgins

editors@sciam.com

March 2011

FREEDOM AND COMMERCE

The commentary by Jonathan Zittrain on "Freedom and Anonymity" [Forum] misses the point. His proposed solution of caching linked pages on referring sites ensures redundancy but not security. The FBI officials who worry about Internet attacks do not care whether I can access WhiteHouse.gov or Wikipedia. Instead they worry about disruption of sites such as Amazon.com, which in 2010 averaged more than $90 million in net sales a day. The linked material on these sites is worth nothing compared with the flow of money and orders to their back-end servers and the value that is inherent in their customers' personal and financial data.

While the Internet plays an important role in spreading ideas and encouraging political thought, it also constitutes a significant fraction of our global economy. It is commerce, not content, that drives the quest for better Internet security.

Brett Pantalone
Pittsboro, N.C.

"It is commerce, not content, that drives the quest for better Internet security."
Brett Pantalone *Pittsboro, N.C.*

TRUE GRIT

In "The Neuroscience of True Grit," Gary Stix points out that the U.S. Army's adaptation of Martin E. P. Seligman's Penn Resiliency Program to assess and improve the "emotional and spiritual" well-being of soldiers is being launched to the tune of $125 million, although its efficacy has not been properly tested. What Stix fails to mention is the impact of this mandatory program on the estimated 25 percent of soldiers who report no religious preference. Soldiers who respond in the negative on such measures as "I am a spiritual person," or "I often find comfort in my religious or spiritual beliefs," or "in difficult times, I pray or meditate," or "I attend religious services [how often?]" receive low spiritual-fitness ratings and are referred to a training program that extols prayer and encourages them to seek religious counseling.

This policy simply assumes that we can infer that the nonreligious lack emotional resources and are less able to cope with stress from the fact that religious people often find solace and strength in their beliefs. Of course, the more important point is that the program amounts to proselytizing by the U.S. government and thus looks like a violation of the First Amendment rights of nonreligious soldiers—to say nothing of being insulting and alienating.

Evan Fales
Iowa City

INSIDE JOBS

In "Financial Flimflam" [Skeptic], Michael Shermer asks and answers only the least interesting of questions about economic predictions. Yes, the largest "actively managed" funds underperform passive ones, largely because of higher fees. Ho hum. Then again, dismissing the entire hedge fund industry because T. Boone Pickens was wrong about wind power is as ridiculous as concluding the opposite because Warren Buffet has routinely outperformed the market. Shermer is well aware of the logical fallacies involved because he quite literally wrote the book on them [*The Mind of the Market,* Holt, 2009].

Far more interesting would be to examine whether or not the claims of successful active managers stand up to scrutiny. For example, many claim that quicker access to and better use of information constitutes an edge. Law-enforcement authorities the world over seem to agree, given their reactions to the use of insider information.

Can an edge be developed legally? Some claim that small size or trading in areas underserved by risk capital can constitute an edge. Is this possible? Some claim that behavioral information is embedded in historical price charts. The list goes on, and some money managers who claim to have an edge would argue that it can persist only in an environment in which most market participants refuse to believe that there is such an advantage and so would thank Shermer for his article. The point is that some money managers consistently outperform the market over many years. Are they simply the beneficiaries of luck?

Jon Blumenfeld
Westport, Conn.

CROPS OF THE FUTURE

Julian P. Sachs and Conor L. Myhrvold acknowledge in "A Shifting Band of Rain" that as the global rain band shifts its position northward, "some places are likely to benefit, but many others, we fear, will face dry times." Then, as with many predictive models of coming climate change, they focus on the detrimental effects of the continuation of such change to human societies and thus seem to advocate a plan A of trying to slow or reverse it. Perhaps it is time to start thinking about plan B: dealing with the results of climate change proactively.

For example, by recognizing that the currently wet areas of the earth will eventually miss a good portion of the Intertropical Convergence Zone (ITCZ) rains they now receive, causing their wet climate crops such as coffee and bananas to no longer thrive, plan B would use this predictive model to encourage countries that will ultimately be within the ITCZ to finance more planting of such crops.

Allen Dart
Tucson, Ariz.

I AM A FORD, I AM A CHEVY

David Pogue is wrong when he writes in "Gadget Politics" [TechnoFiles] that fierce techno loyalty is a recent phenomenon. When I grew up in a small town in Iowa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in the 1950s, there were two great lines of social division: Protestant versus Catholic and Chevy versus Ford. (Plymouth people were too weird to seriously consider.)

Bob Swanson
Pocatello, Idaho

COLD ATOMS

In "Demons, Entropy and the Quest for Absolute Zero," Mark G. Raizen describes experiments in which a one-way laser gate reduces the volume of a gas, and thus lowers its entropy, without increasing its temperature. Raizen points out that the decrease in entropy can be explained by information considerations. Such an explanation is not necessary, however. The construction of the lasers, the power they consume, and the rest of the experimental apparatus all account for a great increase in entropy. I thought that this increase in entropy must be taken into account, and it clearly offsets the drop in entropy he produced. Information flow is not needed to explain the entropy drop.

Michael Bookbinder
New Canaan, Conn.

RAIZEN REPLIES: I restricted the system of interest to a collection of atoms in a box interacting with a laser beam. We are interested only in the change of entropy caused by that interaction. This is commonly done in thermodynamics, and one does not need to take into account all the entropy that went into the production of the laser beam.

ERRATUM

A reader's letter concerning the November 2010 Advances article "Window Shopping for Electric Cars" erroneously stated that a turbo diesel Volkswagen Jetta station wagon sells for $16,000. Its sticker price is close to $25,000.

CLARIFICATION

In "Not Just an Illness of the Rich," Mary Carmichael wrote that by 2020, 15 million people worldwide will have cancer; she was referring to the new cases projected to arise during that year, not to the total number of people afflicted by the disease.

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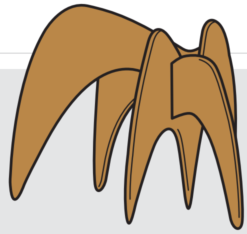

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LETTERS TO THE EDITOR

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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/jul2011

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Physician, Heal the System

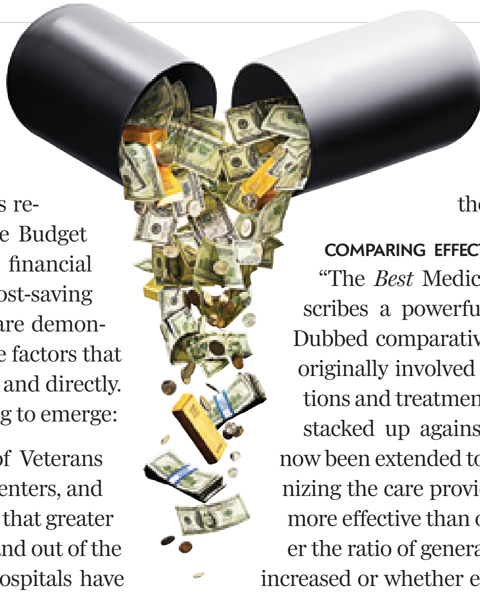
Health care that is fairer and more rational is also more affordable

Two years ago you could scarcely open a newspaper without reading about health care, and you might be forgiven for thinking (or hoping) that the debate was over. Yet the Patient Protection and Affordable Care Act that was signed into law in March 2010 offers more concrete plans for reforming the health *insurance* system than for reforming the health *care* system. It will change *how* we pay for health care but not *how much* we pay—and that is a problem. Government actuaries have calculated that total health care spending by the public and private sectors will grow from $2.7 trillion (17.4 percent of GDP) in 2011 to $4.6 trillion (19.6 percent) in 2019. The U.S. needs to get smarter about restraining soaring medical bills while improving the quality of care.

The U.S. is not alone in facing this dilemma, but it is arguably the most deeply encumbered by it. It spends far more per capita than any other industrial nation, yet all that money fails to buy the best care. In terms of people's level of disability, the care they receive for chronic conditions, and their life expectancy, the U.S. ranks below many other countries that spend much less. Compared with the average American, the average citizen of France or Israel lives three years longer, the average Australian four years, and the average Japanese five years.

Why does health care cost so much more and deliver so much less in the U.S.—and what can be done about it? No single or simple explanation covers all the bases, but three factors loom particularly large. First, the U.S. health care system is highly fragmented, leading to much duplication of effort. A 2007 study, for example, found that older patients see an average of seven different doctors, including five specialists from four different practices, in any given year. Second, clinicians and health organizations are paid on the basis of the services they provide rather than improvements in their patients' health, creating perverse economic incentives to overuse drugs, procedures and hospital beds. Third, doctors and hospitals are quick to adopt expensive new drugs, procedures and technologies without requiring that they prove significantly more effective than cheaper alternatives.

Politicians have acknowledged the crippling cost of medicine, yet their proposals do little to fix these basic flaws. For instance, replacing Medicare benefits with vouchers that individuals can use to buy their own health insurance, as was recently proposed by House Committee on the Budget Chair Paul Ryan, merely shifts more of the financial burden to private citizens. And most of the cost-saving initiatives found in the Affordable Care Act are demonstration projects—not large-scale reforms. The factors that inflate health costs must be addressed widely and directly. Fortunately, promising solutions are beginning to emerge:



REDUCING FRAGMENTATION. The Department of Veterans Affairs, federally certified community health centers, and a few regional care systems are demonstrating that greater coordination of care can keep people healthy and out of the hospital. For example, several Philadelphia hospitals have assigned nurse practitioners to organize the care of elderly patients with chronic illnesses after they were discharged. Readmission rates have dropped by more than a third and net expenditures by nearly 40 percent, despite the extra personnel costs.

PHASING OUT FEE-FOR-SERVICE. So-called accountable care organizations are pairing hospitals with community health teams. These groups will be paid a set amount per patient based on the severity of the individual's condition, such as diabetes. The organization earns a bonus if the person's health improves and keeps any savings if it manages to meet its health targets for less than the contracted amount.

COMPARING EFFECTIVENESS OF PROCEDURES. On page 50, in "The *Best* Medicine," science writer Sharon Begley describes a powerful analytical tool to help rein in cost. Dubbed comparative effectiveness research, this approach originally involved mining the available data about conditions and treatments to figure out how expensive therapies stacked up against cheaper options. The technique has now been extended to determine whether some ways of organizing the care provided by hospitals and health centers are more effective than others. For example, it can check whether the ratio of general care clinicians to specialists should be increased or whether elderly patients would benefit from support services that allow them to live longer at home.

None of these approaches is a magic bullet. Health care is too complex, requiring coordinated efforts on the part of many different individuals, for any single initiative to provide all the answers. Still, they offer powerful, evidence-based tools to control costs in a fair and reasonable manner. They need to be scaled up. Otherwise, chances are that in the future medical care in the U.S. will be crueler, more arbitrary and available only to the wealthy. SA

COMMENT ON THIS ARTICLE ONLINE
ScientificAmerican.com/jul2011

DAN SAELINGER *Getty Images*

Commentary on science in the news from the experts

Timothy Searchinger is a research scholar at Princeton University.

A Quick Fix to the Food Crisis

Curbing biofuels should halt price rises

When food prices rose steeply in 2007 and climaxed in the winter of 2008, politicians and the press decried the impact on the billion or so people who were already going hungry. Excellent growing weather and good harvests provided temporary relief, but prices have once again soared to record heights. This time around people are paying less attention.

The public has a short attention span regarding problems of the world's have-nots, but experts are partly to blame, too. Economists have made such a fuss about how complicated the food crisis is that they have created the impression that it has no ready solution, making it seem like one of those intractable problems, like poverty and disease, that are so easy to stash in the back of our minds. This view is wrong.

To be sure, reducing hunger in a world headed toward more than nine billion people by 2050 is a truly complicated challenge that calls for a broad range of solutions. But this is a long-term problem separate from the sudden rise in food prices. High oil prices and a weaker dollar have played some part by driving up production costs, but they cannot come close to explaining why wholesale food prices have doubled since 2004. The current price surge reflects a shortfall in supply to meet demand, which forces consumers to bid against one another to secure their supplies. Soaring farm profits and land values support this explanation. What explains this imbalance?

Crop production has not slowed: total world grain production last year was the third highest in history. Indeed, it has grown since 2004 at rates that, on average, exceed the long-term trend since 1980 and roughly match the trends of the past decade. Even with bad weather in Russia and northern Australia last year, global average crop yields were only 1 percent below what the trends would lead us to expect, a modest gap.

The problem is therefore one of rapidly rising demand. Conventional wisdom points to Asia as the source, but that's not so. China has contributed somewhat to tighter markets in recent years by importing more soybeans and cutting back on grain exports to build up its stocks, which should serve as a warning to policy makers for the future. But consumption in China and India is rising no faster than it has in previous decades. In general, Asia's higher incomes have not triggered the surge in demand for food.

That starring role belongs to biofuels. Since 2004 biofuels from crops have almost doubled the rate of growth in global demand for grain and sugar and pushed up the yearly growth in demand for vegetable oil by around 40 percent. Even cassava is edging out other crops in Thailand because China uses it to make ethanol.

Increasing demand for corn, wheat, soybeans, sugar, vegetable oil and cassava competes for limited acres of farmland, at least until farmers have had time to plow up more forest and grassland, which means that tightness in one crop market translates to tightness in others. Overall, global agriculture can keep up with growing demand if the weather is favorable, but even the mildly poor 2010 growing season was enough to force a draw down in stockpiles of grain outside China, which sent total grain stocks to very low levels. Low reserves and rising demand for both food and biofuels create the risk of greater shortfalls in supply and send prices skyward.

Although most experts recognize the important role biofuels play, they often underestimate their effects. Many of them misinterpret the economic models, which understate the degree to which biofuels drive up prices. These models are nearly all designed to estimate biofuels' effects on prices over the long term, after farmers have ample time to plow up and plant more land, and do not speak to prices in the shorter term. Commentators also often lump all sources of crop demand together without recognizing their different moral weights and potential for control. Our primary obligation is to feed the hungry. Biofuels are undermining our ability to do so. Governments can stop the recurring pattern of food crises by backing off their demands for ever more biofuels. SA

COMMENT ON THIS ARTICLE ONLINE ScientificAmerican.com/jul2011

JOHN ZOINER *Getty Images*

ENVIRONMENT

Tortoises to the Rescue

Rewilding islands and even continents could prove an effective method for reversing ecological catastrophe

Europeans ate their way through the island nation of Mauritius, most famously eliminating the dodo bird by 1700. Less well known was their effect on the Mauritian island now known as Ile aux Aigrettes, where they exterminated giant skinks and tortoises and logged the native ebony trees for firewood.

In 1965 the largely denuded 25 hectares of the island were declared a nature reserve. But even in the absence of logging, the slow-growing ebony forests failed to thrive. Why? Because they had lost the animals that ate their fruit and dispersed their seeds. So in 2000 scientists relocated four giant tortoises from the nearby Aldabra atoll in the Seychelles, and by 2009 a total of 19 such introduced tortoises roamed the island, eating the large fruits and leaving behind more than 500 dense patches of seedlings. The team reported its results in April in the journal *Current Biology*.

For this tiny island, at least, rewilding appears to have worked. And that holds out hope for other restoration ecology projects in the midst of the sixth mass extinction in the earth's history. In Europe conservationists have received €3.1 million to begin bringing bison, bovines and horses back to "abandoned" agricultural lands in places such as western Spain or the Carpathian Mountains. Ecologists have proposed repopulating parts of the U.S. with elephants, which would replace extinct mastodons. The Dutch, for their part, have already built what amounts to a Pleistocene park at Oostvaardersplassen, adding Konik horses and Heck cattle to replace extinct wild horses and cattle.

Of course, humans have a mixed track record when it comes to interfering in natural ecological systems—the introduction of the cane toad to Australia to manage other pests has resulted in a frog march of havoc across the continent. "There are no guarantees when trying to manipulate nature," notes ecologist Mark A. Davis of Macalester College in Minnesota. Others argue that humans should fix what they have broken. "There is no place on this planet that humans have not interfered with, and it is time for us to become actively involved in engineering solutions," says marine biologist Ove Hoegh-Guldberg of the University of Queensland in Australia. "There are no other options except extinction at this point." *—David Biello*

GARY OMBLER *Darling Kindersley*

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INDICATION:

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

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

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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- People allergic to anything in LIPITOR

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

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

Common side effects of LIPITOR are:

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

HOW TO TAKE LIPITOR

Do:

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

Don't:

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

NEED MORE INFORMATION?

- Ask your doctor or health care provider.
- Talk to your pharmacist.
- Go to **www.lipitor.com** or call **1-888-LIPITOR**.

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Printed in the USA.

Distributed by Parke-Davis, Division of Pfizer Inc.
New York, NY 10017 USA
June 2009

Rx only

Gotcha: A galaxy cluster dominated by dark matter

PHYSICS

International Particle of Mystery

Dark matter escapes its dragnet once again—or does it?

The generic line on dark matter is that nobody knows what it is because nobody has seen it. The former claim remains unassailable—any number of hypothetical particles could be dark matter. As to whether or not anybody has seen it, scientists are as divided as ever, and the discourse among rival dark matter hunters is getting chippy.

The controversy centers on an Italy-based research group that runs DAMA, a particle detector that the researchers have claimed for years is picking up dark matter particles. But the group has been secretive about its data, critics say, and physicists have by and large remained skeptical. Indeed, in April a top experimental collaboration known as XENON100 reported findings that appeared to rule out the possibility that DAMA's signal came from dark matter.

At issue is not the data so much as what they mean. If dark matter rings the galaxy as theory predicts, Earth should be orbiting through a sea of dark particles, and DAMA should detect this as the yearlong ebb and flow in the "ambient particle environment." For more than 10 years now, DAMA has been registering blips that fit this pattern. "I think everyone would agree at this point that they see a signal," astronomer Mario Livio of the Space Telescope Science Institute in Baltimore said in May at a dark matter symposium. "The question is, What is it?"

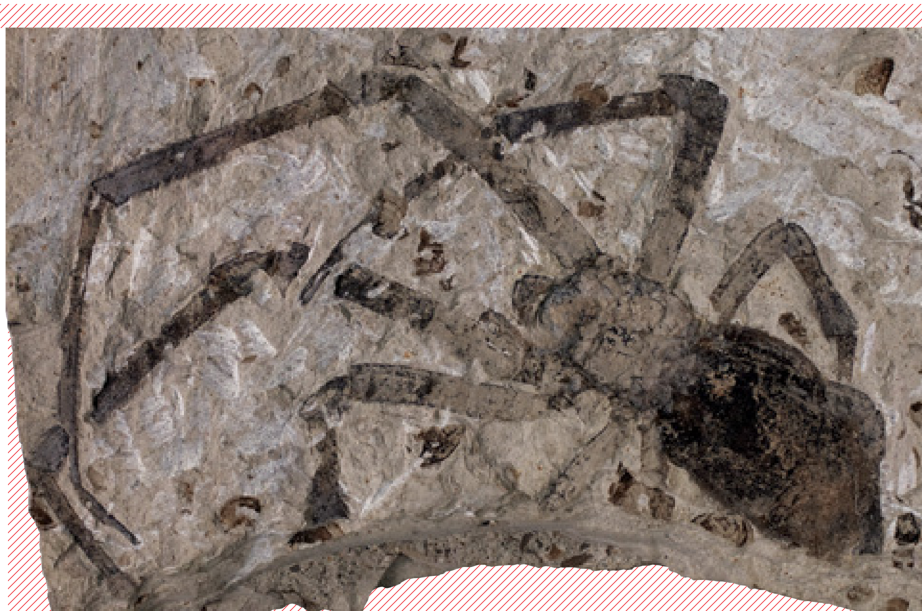
DAMA researchers have now found, at last, some preliminary validation of their claim to have seen signs of dark matter. A Minnesota detector called CoGeNT has registered seasonal blips akin to what DAMA has seen, physicist Juan I. Collar of the University of Chicago said at the symposium. He cautioned that the data are preliminary but charged that competitors—including one whose results he derided as "pure, weapons-grade balonium"—have been too quick to dismiss DAMA.

CoGeNT may turn out to be the ally DAMA has long lacked, but Collar maintains that he is not taking sides. "Maybe DAMA's wrong, maybe they're right, but we have to remain neutral," he said. "I find myself caught between the believers and heathens." The upshot: the field of dark matter research remains as murky as ever.

—John Matson

WHAT IS IT?

Charlotte's ancestor: Thanks to a chance find by farmers in Inner Mongolia, scientists have learned that today's largest web-weaving spiders are about 130 million years older than previously thought. In 2005 Chinese farmers digging in ancient volcanic ash unearthed the fossil at the right, the biggest spider fossil ever discovered and one of the best preserved. Paul A. Selden, director of the University of Kansas Paleontological Institute, and his colleagues, writing in April in the online *Biology Letters,* report that the female spider, a member of the *Nephila* genus, measures nearly one inch in length, has a leg span of more than five inches and is 165 million years old. "Extremely fine details, such as sensory hairs called trichobothria, which the spider uses to detect air vibrations, can be seen," Selden says. No word on her ability to write "Some pig." *—Ann Chin*



X-RAY: NASA/CXC/M. MARKEVITCH ET AL.; OPTICAL: NASA/STSCI, MAGELLAN/U. ARIZONA/D. CLOWE ET AL.; LENSING MAP: NASA/STSCI, ESO WFI, MAGELLAN/U. ARIZONA/D. CLOWE ET AL. (*cluster*); PAUL A. SELDEN (*spider*)

COURTESY OF DISNEY/PIXAR

ENTERTAINMENT

Light at the End of the Racetrack

How Pixar explored the physics of light for *Cars 2*

Although the stories told by Pixar Animation Studios take place in richly realized fantasy realms, the science and technology required to create those worlds have distinctly real-world origins.

For *Cars 2,* set for release in late June, the minds behind such films as *Toy Story, Up* and *WALL-E* had to study the complex ways in which light reflects off cars. The movie leaves behind the sleepy desert town setting of the original and takes place in the world of international racing, which meant having to depict many cars moving through varied tracks and racing surfaces. Producers quickly realized that Pixar's existing 3-D lighting system would need significant upgrading.

"Cars are designed and painted to have a unique relationship to color and light," says Pixar lighting team member Sudeep Rangaswamy. "So we needed to explore how light plays off of fast-moving vehicles—and how their movement and reflective qualities play off of the surrounding environment."

A research team at Pixar studied the light-absorbing qualities of auto paint, carbon fiber and chrome, as well as the darkness-penetrating intensity and reach of standard and LCD headlights. The results were programmed into algorithms that calculate and render in real time the frequency and temperature of light and color on reflective, absorbing and distorting materials.

That research was then integrated into a new lighting engine—software that allows animators to create scenes that appear to be illuminated from any angle, just the kind of effect a real-world director of photography would aim for. The lighting engine integrates with a virtual camera system, which allowed director John Lasseter to create scenes from any camera perspective. "The new engine allows lights from the scene to interact correctly with the characters the animators place within it," Rangaswamy says. "For example, we re-created downtown Tokyo for the film with all its neon lights. The engine created those lights with its [artificial intelligence] and maintained them—automatically, creating the correct lighting relationships."

Thus, as Lightning McQueen races, the track lights and neon signs reflect off of his red paint, and that red glow can now reflect in a puddle as he passes, which alters the color of the car next to him—all without the animators needing to render these effects "by hand" from scene to scene. The new lighting technology will remain in Pixar's proprietary software toolbox for future films long after *Cars 2* rolls over the horizon.

—John Scott Lewinski

COMMENT AT ScientificAmerican.com/jul2011

MEDICINE

Itch Doctor

The head of a new center that focuses on itch explains the sensation's biological roots and what we still don't know about it

PROFILE

NAME
Zhou-Feng Chen

TITLE
Director, Center for the Study of Itch at the Washington University School of Medicine

LOCATION
St. Louis, Mo.

Why do we need a research center dedicated to itch?
First, chronic itch is a major underreported disease. Many patients—as many as 17 percent of adults, according to one study—suffer from it, and many of them never seek medical help. They think they can scratch it away. Because it's not cancer, you don't die from it, so people don't take it seriously. But a majority of chronic itch is resistant to treatment.

What causes it?
It can be associated with a skin condition such as psoriasis, or it can stem from a systemic disease, such as kidney or liver failure. It can also be a side effect of chemotherapy. Other times it is caused by a deregulation of the nervous system: something is wrong with the nervous system and the itch pathway is activated.

Tell me about your current research.
We are trying to understand how our nervous system transmits the itch signal. Three years ago we identified a subset of neurons in the mouse spinal cord through which all itch sensations pass. This raises very interesting possibilities. If those same kinds of neurons exist in the human spinal cord, and if you could block that molecular signaling pathway, you might stop itch transmission and greatly improve someone's quality of life.

What is the relation between itch and pain?
For a long time, people thought itch and pain were transmitted through the same pathway, that itch was just a weaker form of pain. But now we know that they are transmitted through separate pathways and that they also antagonize each other: when you create pain, you can suppress itch, like when you scratch.

Also, their biological functions are different. When you feel pain, you withdraw to protect yourself. But when you feel an itch, you move your hands toward it. If something attaches itself to your skin, like a mosquito, you want to remove it. So it is possible that the body's warning system is telling you that something is happening to your skin and that you'd better get rid of it.

What are the main unanswered questions in your field?
We want to know how the itch sensation is caused in the first place. Our discovery of an itch receptor called GRPR and itch-specific neurons was just the first step. The system is so complex that we still don't know how this information flows in the body, and we also don't know how different kinds of diseases activate the itch receptor. There are receptors located in the skin, in the brain and in the spinal cord, so it's extremely complicated. That's why we need more scientists in different areas working together.

—*Interview by Anna Kuchment*

QUOTABLE

"I wouldn't compare it to sex, but it lasts longer."

—British physicist Stephen Hawking, speaking about the joys of scientific discovery at Arizona State University in April.

COURTESY OF ELISA YIN

Urge to merge: Columbia's new science building

RESEARCH

Big Buzzword on Campus

Is "convergence" a revolution in science or jargon?

Research universities have been abuzz with what some are calling the "next big thing": convergence, the integration of the life, engineering and physical sciences. This wholesale merging of minds is being billed as critical to helping researchers answer the most profound questions: How does the brain work? What causes cancer? How can we make energy more sustainable? "The convergence revolution is a paradigm shift," write the authors of a recent white paper from the Massachusetts Institute of Technology. "Convergence means a broad rethinking of how all scientific research can be conducted."

Researchers can be forgiven for thinking they have heard this all before. The concept of merging tools and methods from separate disciplines is not new; the x-ray's arrival in 1895 brought physics to the doctor's office. More recently, the Human Genome Project spawned integrated fields such as bioinformatics and systems biology. But Phillip A. Sharp, a biology professor at M.I.T. and co-author of the white paper, argues that the true multidisciplinary nature of convergence marks a "third revolution" in science that is following in the footsteps of the molecular biology revolution of the 1950s and the genomics revolution that began in the late 1980s.

If something revolutionary is again afoot, it has only recently begun reaching critical mass, with more universities opening facilities and revamping hiring practices to foster cross-disciplinary research. Earlier this year New York University cut the ribbon on its Biomedical Chemistry Institute, with laboratories shared by chemists and biomedical researchers collaborating on new antibiotics, malaria drugs and cancer diagnostics. M.I.T.'s new David H. Koch Institute for Integrative Cancer Research mixes biology and engineering labs and features common spaces designed to promote interaction. Columbia University's recently opened Northwest Corner Building brings together engineers, physicists, chemists and biologists in open-format labs and a common dining hall and library. Other universities have started recruiting across disciplines. Michigan Technological University has experimented with hiring faculty by research theme—such as energy—rather than by department. And last October the University of Iowa announced 14 new tenure-track positions as part of a multidisciplinary hiring initiative centered on "the aging mind and brain."

So is convergence a revolution or simply a matter of scientific evolution? It may be hard to tell until it yields its own version of the double helix or the human genome. *—Bryn Nelson*

PATENT WATCH

Device for avoiding a collision in a lane-change maneuver of a vehicle: It's not quite KITT, the artificially intelligent Trans Am that starred alongside David Hasselhoff in the 1980s television show *Knight Rider,* but a newly patented computerized driving system takes a step toward the car as driving companion. Not only will it upbraid you when you are about to make a boneheaded lane change, it will actually take control of the steering wheel and prevent a collision.

The device, patent No. 7,893,89, was developed by a team of engineers at Germany's Continental Corporation. It relies on cameras embedded in a car's side mirrors. The cameras stream video to a computer, perhaps located behind the dashboard, equipped with object-recognition software that scans every 66 milliseconds for the shapes of approaching vehicles. Once it identifies a vehicle, the system tracks the approaching car's changing geometric relation to other visual cues on the horizon to determine its approach speed and distance.

When a driver begins to make a turn into a neighboring lane that the computer believes will result in a collision, it delivers a warning message, "acoustically, visually or both in parallel," says Stefan Lüke, the lead engineer on the project. If that warning is ignored, the computer will deliver another caution through vibrations in the steering wheel. It will then add additional resistance and finally apply countertorque to the steering column, effectively preventing the car from changing lanes. "It feels like driving against a wall," Lüke says. "It will push you back into your lane."

BMW recently debuted a system that tracks approaching vehicles using radar and applies a warning vibration to the steering column. But it does not have the capacity to push the car back into its lane. Lüke predicts that Continental's version, which also works with radar, will appear in its first vehicle "within the year," although he declines to name the model or car manufacturer that plans to deploy it.

The emergence of electromechanical steering systems, which are increasingly replacing traditional hydraulics in vehicles, makes such computerized interventions easier to implement. Meanwhile high-resolution cameras continue to drop in price, making the system more cost-effective, Lüke says. Soon all that will separate your average driver from the 1980s-era Michael Knight will be a "turbo boost" and a few cans of hair spray.
—Adam Piore

COURTESY OF MICHAEL MORAN *(building)*; WALTER GIORDANI *Getty Images (car)*

COMMENT AT ScientificAmerican.com/jul2011

In the weeds: Cogongrass at work

ECOLOGY

A Wild, Weedy Scourge

The federal government is spending millions to combat a nasty plant that is spreading like wildfire

As a single plant, cogongrass is unassuming, bucolic even. But in dense stands, it is a powerful vegetative force that alters forests and forges monocultures. The plant, known as *Imperata cylindrica,* has established itself on tens of thousands of acres in Alabama, Mississippi and Georgia and on one million acres in Florida, and it's spreading fast. "Cogongrass could become a greater threat than kudzu or Japanese honeysuckle," says Stephen Enloe, an invasive plant specialist at Alabama's Auburn University.

Cogongrass not only forms into thick mats of thatch and leaves that make it nearly impossible for native plants to survive, but it also burns hotter than native species. After a burn, a six- to 12-inch-deep rhizome network sends up new shoots, regenerating themselves as soon as a month after the fire. This resilience makes it a severe threat to forests, especially the pine stands that make up a major industry in the South. Cogongrass is estimated to cost Alabama alone more than $7.5 million per year in lost timber productivity.

Heeding the call of worried scientists and others, the federal government has spent millions in American Reinvestment and Recovery Act money to fight the weedy scourge. These funds are being used to detect and treat infested areas of cogongrass, says Stephen Pecot of the Alabama Cogongrass Control Center.

Very few methods fight cogongrass effectively, so researchers are developing new ones. Investigators are testing herbicides, deploying remote-sensing techniques for mapping large infestations and detecting incipient patches that may be obscured by trees or shrubs, and studying cogongrass genetics to better understand the plants across their U.S. range.

A study published in May in the *American Naturalist* reported that plants such as cogongrass grow best in nitrogen-rich soil, suggesting that lowering the nitrogen content—perhaps by boosting the number of nitrogen-devouring microbes in the soil—might work. Says Enloe: "With persistence, it can be dealt with, but it requires a lot of land managers to kick it up a notch."

—Carrie Madren

PSYCHOLOGY

Beauty and the Beasts

The sight of a pretty woman can make men crave war

Show a man a picture of an attractive woman, and he might play riskier blackjack. With a real-life pretty woman watching, he might cross traffic against a red light. Such exhibitions of agility and bravado are the behavioral equivalent in humans of physical attributes such as antlers and horns in animals. "Mate with me," they signal to women. "I can brave danger to defend you and the children."

So says Lei Chang, a psychologist at the Chinese University of Hong Kong. With colleagues there and at China's Hebei University, Chang wondered whether military weaponry and paraphernalia hold the same seductive value as antlers, horns and risky behavior, allowing warriors to best nonwarriors in the competition for mates. The researchers also speculated about war itself. When raping and pillaging, armies resemble chimps on intergroup sex raids. Might warfare actually be driven by the opportunity it offers males to impregnate females, willing and not willing?

To begin to address such questions, Chang showed men pictures of women and tested for statistically significant effects of those pictures on men's attitudes about war and on their cognitive processes related to war. As he and his colleagues describe in the online March 23 *Personality and Social Psychology Bulletin,* they asked the men to rate their agreement with war-supporting statements. Men's responses demonstrated a positive, significant statistical correlation between seeing photographs of attractive faces and endorsing war-supporting statements. This correlation was not demonstrated for photographs of unattractive women's faces, and the researchers found no statistically significant effect on women of pictures of either attractive or unattractive men in any measure related to war.

Chang and his colleagues suggest that any warring-mating relation in men is probably an evolutionary holdover from pre–*Homo sapiens* days, which explains why raping and pillaging are, unfortunately, alive and well. *—Rebecca Coffey*

NIGEL CATTLIN *Photo Researchers, Inc.*

Illustrations by Thomas Fuchs

MEDICINE

Donor Fatigue

The Red Cross has banned chronic fatigue syndrome sufferers from giving blood. But does a virus really cause the disease?

Scientists may still be debating the role of viruses in chronic fatigue syndrome, but blood banks aren't taking any chances. Last summer the AABB, a nonprofit that represents blood-collecting organizations, advised people with the disorder, marked by severe fatigue and aches lasting six months or more, to self-defer from blood donation. Last December the American Red Cross went further, banning people who revealed during a predonation interview that they had the syndrome from ever giving blood at its centers.

The cause for this abundance of caution is XMRV (xenotropic murine leukemia virus–related virus), a retrovirus that has been associated with chronic fatigue syndrome. In a highly publicized 2009 study published in *Science,* XMRV was found in 67 percent of patients and 3.7 percent of healthy controls. But subsequent studies failed to find the virus in people with or without the syndrome, suggesting to some that XMRV may be a laboratory contaminant that skewed the initial trial.

How worried should one be about XMRV in the blood supply? Not very. There has been no evidence of anyone contracting chronic fatigue syndrome from a blood transfusion, so the risk is hypothetical. And more stringent measures, such as screening potential donors for the syndrome via questionnaire, would take attention away from diseases such as HIV and hepatitis B that are unequivocally blood-borne, says Harvey Klein, chair of the AABB task force examining this issue.

Still, experts are weighing whether or not to test donated blood. The first step in that process is agreeing on a standard method for detecting the virus in the blood. A team at the National Heart, Lung, and Blood Institute is comparing the different nucleic acid tests and blood-sample preparation techniques used by various labs—including the Centers for Disease Control and the Food and Drug Administration—to find the best one.

If the test that comes out on top confirms the results of the 2009 study, that is, if it consistently detects XMRV in blood samples from chronic fatigue syndrome patients and does not detect it in negative controls, "we will have identified sensitive and specific methods to detect XMRV in blood samples," says Simone Glynn, who chairs the NHLBI working group overseeing the study.

The next step would be to use that test to check for the presence of XMRV in large numbers of blood donor samples. If the virus is prevalent, the team would examine frozen blood samples and check for evidence of transfusion transmission. "Conversely, if we do not find evidence of XMRV in the blood samples from patients with chronic fatigue syndrome who were previously found to be positive, we would conclude that these viruses do not appear to be present in blood," Glynn says.

For now, excluding people with the syndrome from blood donation is prudent, says Ian Lipkin, director of the Center for Infection and Immunity at the Columbia University Mailman School of Public Health, who is heading the National Institutes of Health–funded investigation into the connection between chronic fatigue syndrome and XMRV. "My sense is that the number of people with the syndrome likely to be sufficiently fit to make blood donations is so few that the Red Cross and AABB have decided for a variety of reasons, scientific and otherwise that it's just not worth the risk." *—Nina Bai*

TIME & LIFE PICTURES/GETTY IMAGES (*Mohammed*); CRACK PALINGGI *Reuters* (*Samudra*); AP PHOTO (*bin Laden*)

SECURITY

Al Qaeda and the Internet

Why the terrorist group has failed in its attempts at cyberwarfare

Will al Qaeda respond to the death of Osama bin Laden with serious cyberattacks? The short answer is no. Despite an active interest in cyberattacks, al Qaeda has not managed any successful assaults other than some posting of propaganda, ATM milking and credit-card fraud. This is mainly because its key computer experts have been captured or killed. Here we reconstruct the group's efforts to tamper with Western technology:

1999 — 2000 — 2001 — 2002 — 2003 — 2004 — 2005

July 1999: The first cyberconflict between Hamas and Israel inspires al Qaeda's leaders, including Khalid Shaikh Mohammed.

June 2002: American officials warn that hackers associated with al Qaeda have been accessing hacker tools and probing emergency phone systems, nuclear power facilities, water systems and gas pipelines.

November 2002: Imam Samudra, an advocate of cyberattacks who organized the Bali nightclub bombing, is arrested in Indonesia (and eventually executed).

March 2003: Khalid Shaikh Mohammed is captured in Pakistan. He is currently being held at Guantanamo Bay in Cuba.

COMMENT AT ScientificAmerican.com/jul2011

FOOD

Ultrasonic French Fries

Smooth and crispy

RYAN MATTHEW SMITH *Modernist Cuisine LLC*

It's one of the most commonly consumed snacks in the Western world and has been made in one form or another for at least three centuries, so you might think nothing new could come of the humble french fry. But British chef Heston Blumenthal put paid to that notion years ago. He and his research chef Chris Young came up with a triple-cooked "chip" with a taste and texture that blow away anything you will find at a burger joint. Other chefs have raised the bar further. Nils Norén and Dave Arnold of the French Culinary Institute in New York City, building on work by a Polish researcher, figured out how to improve the texture inside fries by treating the potatoes with an enzyme. The chemical helps break apart the pectin in the fries, yielding a smoother mouthfeel.

Inspired by these heroic efforts, Maxime Bilet, Johnny Zhu and the other research chefs (including Young) at our culinary lab in Bellevue, Wash., explored a variety of techniques for doing better still. The winning combination is simple in its ingredients but quite fancy in its execution. The potato batons are vacuum-sealed with 2 percent salt brine in bags to keep them intact during boiling. They are then bombarded with intense sound waves from the same device that dentists and jewelers use. A lengthy ultrasound treatment at 40 kilohertz causes the surface of each fry to crack and blister with myriad tiny bubbles and fissures.

The cook next vacuum-dries the pretreated potato sticks to adjust the water content of the exterior and then briefly blanches them in oil at 340 degrees Fahrenheit to tighten their network of interlaced starch molecules. After cooling comes the final step: a quick plunge into hot oil at 375 degrees F. Water flashes to steam inside each minuscule bubble on the surface of the fries, expanding in volume by a factor of more than 1,000 and forcing the bubbles to puff up. In just a few minutes of deep frying, the french fries take on an almost furry appearance.

These wonders of 21st-century cooking are unlike any fries you have tried before. A hugely satisfying crunch when you bite through the exterior yields to a center of incredibly smooth mashed-potato consistency. Although there are several steps involved in the process, it is amenable to automation by a food manufacturer. So maybe one day you won't have to settle for flaccid, featureless fries with your fast-food meal.

—W. Wayt Gibbs and Nathan Myhrvold

Myhrvold is author and Gibbs is editor of Modernist Cuisine: The Art and Science of Cooking *(The Cooking Lab, 2011).*

October 2005: Tsouli is arrested in London.

May 2011: U.S. forces find and kill Osama bin Laden in Abbottobad, Pakistan. *—Scott Borg*

Borg is director of the U.S. Cyber Consequences Unit, a nonprofit research institute.

2006 2007 2008 2009 2010 2011 2012

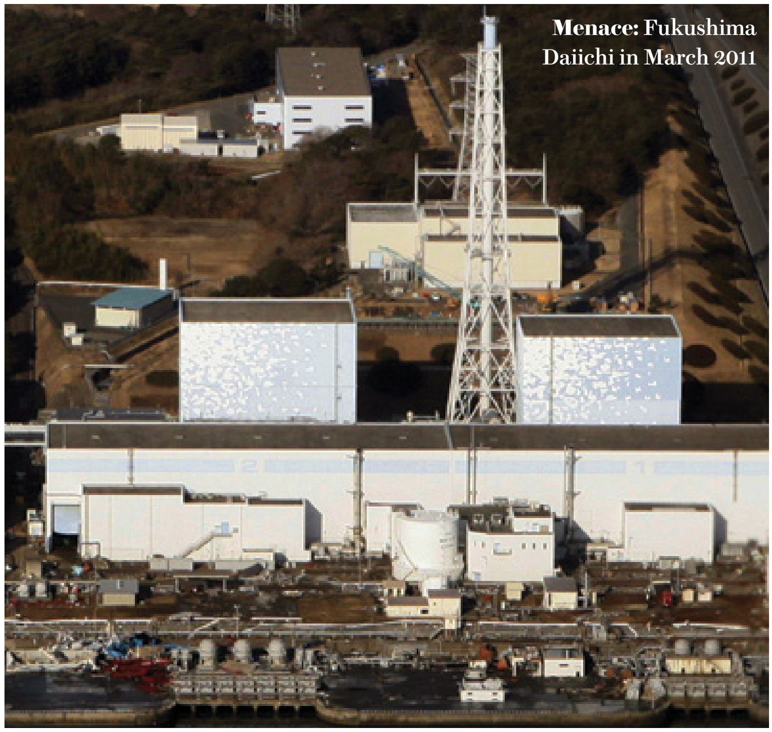
April 2004: Younis Tsouli begins hacking into Web sites to post al Qaeda propaganda. He later distributes a written "Seminar on Hacking Websites" and goes on to perpetrate the most successful al Qaeda–linked cyberattacks to date.

August 2008: One of the last al Qaeda leaders expert in computers, Fazul Abdullah Mohammed, is reported at large in Kenya, but all al Qaeda efforts to mount cyberattacks have died down.

ENERGY

From Nuclear Plant to Nuclear Park?

What the future holds for Japan's Fukushima Daiichi plant



Menace: Fukushima Daiichi in March 2011

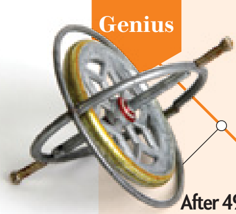
Twenty-five years after the tragedy at the Chernobyl power plant in Ukraine, tons of concrete shield workers and visitors from the puddle of dangerously radioactive melted fuel that lurks in the basement. In contrast, more than 30 years after the accident at Three Mile Island near Harrisburg, Pa., the next-door twin of the partially melted-down reactor is still in operation and surrounded by homes. Eventually the plant will be torn down and the site cleaned up.

These two scenarios—continued operation followed by cleanup versus abandoning and entombing the site—bookend the possible outcomes for the newest member of the nuclear meltdown club, Fukushima Daiichi. The Japanese plant has endured partial meltdowns in at least three of its six reactors, as well as two of its seven pools for storing spent fuel. "You have several [impacted] reactors, and you could easily have two or three approaches to decommissioning," says Kurt Kehler, vice president of decommissioning and demolition at CH2M HILL in Englewood, Colo.

Fukushima's fate will ultimately come down to how badly the fuel at the plant melted, how deeply contaminated the site has become and how much money the Japanese government is willing to spend on cleanup. Tokyo Electric Power, which operates the plant, estimates that the fuel in at least one of the reactors has completely melted down. If so, the fuel rods may have formed a "puddle," not unlike the one at Chernobyl that has necessitated a massive steel structure to contain it. Moreover, radioactive contamination has spread to a 30-kilometer radius of the stricken plant, including to towns even farther afield, such as Iitate, which is so contaminated that it will have to be abandoned or its soil scooped up and entirely replaced. Some 80,000 residents in similar towns have been evacuated.

The Japanese government has called for the plant to be torn down. TEPCO would prefer to restart the undamaged reactors if at all possible. Unfortunately, neither may get its wish: if the fuel has indeed formed a puddle, radiation levels may be too high for would-be deconstruction workers to approach, necessitating entombment efforts similar to those at Chernobyl. And like the Ukrainians and Belarusians who never returned to the exclusion zone, residents in the towns near Fukushima Daiichi may never return home permanently, and local farmers and fisherfolk may not be able to resume their professions. In short, the area surrounding Fukushima may remain a no-go zone for years to come—another name on the list of unexpected nuclear parks and another reminder of the peril of nuclear energy. *—David Biello*

NEWS SCAN



Genius

Intel announced the biggest breakthrough in computer chips in 50 years: "3-D transistors" that, like skyscrapers, pack more punch into less space.

Armadillos, one of the only animals other than humans to carry leprosy, have been spreading the rare bacterial disease in the southern U.S. Stay away from that roadkill.

The gray wolf is removed from the endangered species list in several states as a government shutdown–averting deal, a detail that was most likely lost on the wolves.

After 49 years and $750 million, a Stanford University experiment using superconducting niobium spheres confirmed parts of Einstein's general theory of relativity. Do not try this at home.

Urban birds have bigger brains than other species, making it easier for them to thrive in challenging environments, like Times Square.

Just as we're discovering more Earth-like planets, budget cuts force the shutdown of SETI's array of antennas that hunt for extraterrestrial life. Sorry, E.T. *—George Hackett*

Folly

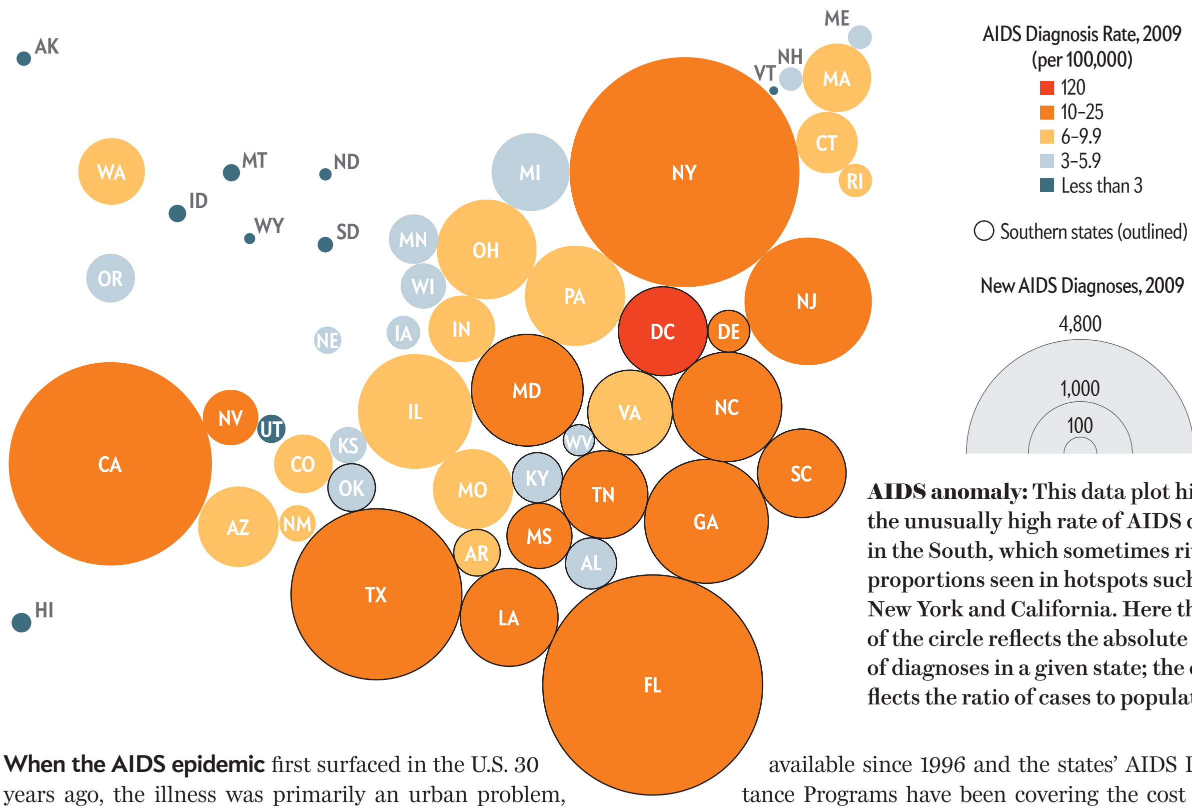
GETTY IMAGES (*Fukushima*); PHOTO RESEARCHERS, INC. (*gyroscope*); JOEL SARTORE *Getty Images* (*armadillo*); SETH SHOSTAK *Photo Researchers, Inc.* (*radio telescope antenna*)

COMMENT AT ScientificAmerican.com/jul2011

Jessica Wapner is based in New York City and writes frequently about biomedical issues.

Poor Man's Burden

Why are HIV rates so distressingly high in the southern U.S.?



AIDS anomaly: This data plot highlights the unusually high rate of AIDS diagnoses in the South, which sometimes rivals the proportions seen in hotspots such as New York and California. Here the size of the circle reflects the absolute number of diagnoses in a given state; the color reflects the ratio of cases to population.

SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION *HIV SURVEILLANCE REPORT*, VOL. 21; 2009

When the AIDS epidemic first surfaced in the U.S. 30 years ago, the illness was primarily an urban problem, centered in cities such as New York, San Francisco and Los Angeles. Today New York State and California still rank among the highest in the number of cases, according to the Centers for Disease Control and Prevention, with more than 150,000 people living with AIDS (the later stages of HIV infection) between them. But in recent years HIV has begun to take a disproportionate toll on the southern U.S., including in rural areas. Despite making up 37 percent of the population, the 16 states plus the District of Columbia that constitute the American South accounted for half of the 45,000 new cases of HIV infection in the U.S. in 2009. Moreover, the South has the highest rate of newly reported infections and the highest number of deaths caused by AIDS.

This regional anomaly has set off alarm bells at state and federal health departments alike, because it shows that current efforts are failing to contain the infection. Considering all that is now known about how HIV is transmitted and how it can be prevented, the rate of new infections should be falling rapidly. Furthermore, deaths should be declining as well because combination therapy that inhibits the progress of the disease has been available since 1996 and the states' AIDS Drug Assistance Programs have been covering the cost of care for many people who can least afford it since 1987. Nor is there anything unusual about the way HIV spreads in the South. Unprotected sex between men remains the most common method of transmission, followed by sharing contaminated needles or having sex with people who fall into either of those categories.

What explains the disturbing numbers, and what can be done about them? Research has identified several interrelated causes—among them poverty, culture and prejudice. Now a few states in the area are attempting to turn the findings into helpful programs. Surprisingly, Mississippi, a state whose many failings in the struggle against AIDS were well documented in a recent 59-page report by Human Rights Watch, could help show the way—although plenty of pitfalls remain.

FACING A STACKED DECK

HIV is, of course, not the only health problem that looms large in the South. The region has long suffered more than its fair share of diabetes, heart disease, certain types of cancer and obesity compared with the Northeast, Midwest and West. As with all these

Graphic by XNR Productions

other health problems, however, addressing the HIV epidemic in the southern U.S. requires much more than just having effective and affordable medicine. It demands an understanding of why individuals in the South turn out to be particularly likely both to delay testing and to seek medical attention only in the later stages of HIV infection, when it is most difficult to treat.

One reason seems to be the strong stigma in the South attached to HIV infection and AIDS, an attitude that is reinforced by many cultural and religious attitudes against homosexuality. Indeed, some young HIV-positive men say they would rather pretend to have a heroin habit than let anyone think they had slept with another man. In response, those at risk often shun testing, and people who do test positive for HIV tend to hide their status until their health deteriorates beyond denial. Meanwhile the virus continues to spread.

Poverty, says Kevin Fenton, director of the CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, is another major cause for delay in testing and treatment. (Mississippi is the poorest state in the Union, according to the U.S. Census Bureau, followed by West Virginia, Arkansas and South Carolina). For people who have little money, HIV may seem like the least of their worries as they struggle to find food, buy clothes and keep a roof over their heads. Many cannot afford health insurance but still make too much money at their low-paying jobs to qualify for Medicaid and other free or low-cost health care benefits. These hassles of everyday living lead large numbers of infected individuals to put off medical care until they are seriously ill.

Even when HIV-positive Southerners do attempt to find care, they often have difficulty getting the treatment they need. Federal government surveys have found that more than half of all people living with HIV in many southern states do not get adequate treatment—compared with a third in other regions. For one thing, states sometimes impose payment rules that tie doctors' hands. Mississippi's Medicaid program, for example, limits beneficiaries (including those with HIV) to just five prescription drugs per month, despite the fact that it often takes many more medications to keep viral levels in check. A sheer lack of doctors plays a part as well. Mississippi has one of the lowest ratios of primary care physicians to resident population in the country. (Primary care clinicians handle the health problems that most people have most of the time.) And practitioners may not be eager to see infected individuals. The Human Rights Watch report included anonymous testimony from clinical workers that many health care practitioners in Mississippi refuse to treat HIV-positive individuals, resulting in long waiting lists for those willing to see such patients. Yet research shows that early treatment improves outcomes, lowers the cost of care and diminishes risky behavior. "People who are in care tend to know more and tend to have less unprotected sex," says Deborah J. Konkle-Parker, associate professor in the department of medicine and infectious diseases at the University of Mississippi Medical Center.

One group that has been especially hard-hit by HIV's ties to poverty and prejudice in recent years is African-Americans. More than half of all households that are poor and black are in the South. Public health experts report that black men who have sex with other men are particularly unlikely to think of themselves as homosexual or at risk for HIV and therefore deny the need for condoms, which reduce the transmission of the virus. Among black men who have sex with men, more new cases of AIDS were diagnosed in the South in 2006 than in all other regions of the country combined. In Mississippi, state health officials report that the number of new cases of HIV among black men aged 13 to 31 years who had sex with other men rose by 48 percent from 2005 to 2007.

MOVING FORWARD

Money cannot cure all the obstacles to improving the HIV picture in the South, but it could certainly help. In July 2010 the Obama administration issued a national strategic plan to tackle HIV in the country's hardest-hit regions, including the South. Increases in funding were announced in February 2011. But with cuts looming in spending on Medicaid, which is paid for by state and federal governments, the people who most need help may end up not getting much more assistance after all.

In the meantime, some states are trying to innovate on their own. South Carolina has an HIV education program that aims to reduce stigma by reaching out to churches and ministers. Arkansas, for the first time, has allotted funds to test the feasibility of offering routine HIV screening to the general population. And Mississippi has zeroed in on what might seem like a surprising solution for a state in the Bible Belt: in March the state passed a law requiring school districts to offer sex education. Nick Mosca, who was appointed director of Mississippi's program for addressing sexually transmitted diseases and HIV a few months earlier, and Mary Currier, the state's health officer, argue that sex education is a top priority—and with good reason. Seventy-five percent of the state's high school seniors report being sexually active, and one in four new HIV cases occurred in young people between the ages of 13 and 24 years.

> Poverty, culture and prejudice help to explain the high number of HIV cases in the southern U.S.

Mosca also hopes to work with Mississippi's Department of Education to begin testing all students in selected high schools for HIV, whether or not they appear to fall into a high-risk group. The move would help anyone who is HIV-positive and does not know it to get treatment. But testing everyone also acts to diffuse any stigma that might be attached to HIV screening because no one is singled out.

Improving access to health care will probably take longer. The Prevention and Public Health Fund, a component of the Affordable Care Act, has allotted $198 million toward training 500 new primary care physicians and 600 new primary care nurse practitioners across the country by 2015. But Governor Haley Barbour of Mississippi has argued that the state does not need the kind of assistance that the law provides. For now the state's health experts hope that their education and testing initiatives can help lessen the alarmingly high rates of HIV infection and death in the U.S.'s poorest state. They have their work cut out for them. SA

SEE ANIMATED AIDS DATA ONLINE
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Does anyone consult "how to" books to learn to walk, run, or ride a bicycle? Do children know they are conforming to natural laws, as they perform those feats? No, of course not! Whoever or whatever created those laws waited untold centuries for people to identify the laws of physics.

There is a natural law of behavior that was not identified until the past century by Richard W. Wetherill. It calls for people's thinking and behavior to be rational and honest, according to the dictates of a self-enforcing natural law.

Wetherill spent decades trying to explain that the social, health, and economic woes of mankind were being caused by people's contradiction of a natural law: a law he called the ***law of absolute right***.

In general, people resent being told what they can and cannot think, say, and do. Their reason seems to be that it is "their business": a mistake made by those who overlook where the gift of life originates.

Introduction to the law of absolute right and its influence on behavior is vital information urgently needed by every member of society.

Strange as it might seem, it could be said, the only choice people have is whether they will live in accord with the dictates of natural laws or be penalized for ignoring them.

Researchers diligently sought to learn of natural laws and how they functioned in order to avoid penalties for ignoring them. So people surrender to laws of physics, telling them what they can and cannot do.

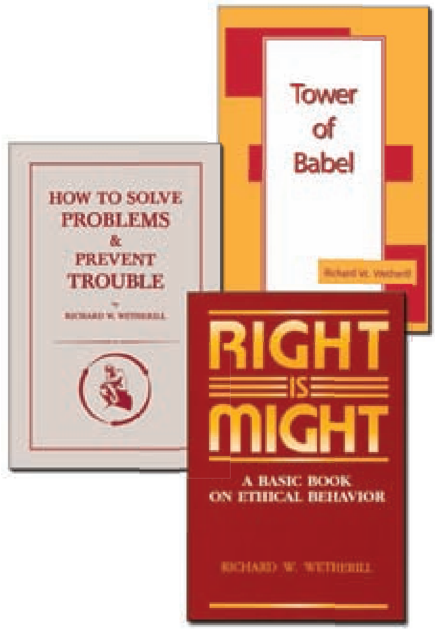
But to date, those researchers' failure to acknowledge nature's law of absolute right and its impact on human life is perpetuating countless human miseries.

We suggest that the behavioral law is nature's way to create a group of survivors that have resolved their former problems and trouble. Having adjusted their decisions to be rational and honest, a common comment heard from those persons is, "It works."

For example, one person reported that he had made friendly overtures to a long-time estranged, close relative and introduced him to the law of absolute right. Later this person reported a phone call from his formerly estranged relative who agreed with others and said, "It works."

We invite readers to face all future situations with a decision to respond rationally and honestly despite any past reactions. In that moment you will have yielded to yet another of nature's laws. And you will discover that it works.

By conforming to nature's law of absolute right, you join other people already enthusiastically benefiting from having changed their former motivation. All it takes is to be rational and honest in all your thoughts, words, and deeds.



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This public-service message is from a self-financed, nonprofit group of former students of Mr. Wetherill.

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

Why Gadgets Flop

A few lessons from the consumer electronics industry's most notorious failures

According to the old saying, you learn more from a failure than a success. Well, if that's the case, the consumer electronics industry ought to have a master's degree by now. There was the ROKR E1 from Apple and Motorola, the first iTunes phone that, idiotically, held a maximum of 100 songs. There was Google Wave, a piece of Web software more baffling and complex than the 1040 tax form. There was the KIN smartphone, which Microsoft spent several years and around $1 billion to develop, only to withdraw it from the market after only two months.

(Not to harp on Microsoft, but let's not forget its SPOT wireless watch, Smart Display wireless screen or Zune wireless music player. In fact, besides the Xbox and PC peripherals, has Microsoft *ever* successfully launched a new piece of hardware?)

When a Hollywood studio sees that a finished movie is awful, it saves itself millions of dollars in marketing and distribution costs by burying it in a closet somewhere. Why doesn't the tech industry follow suit? Could it be that these companies don't realize that their products will tank?

That seems hard to believe. Almost anyone can identify these turkeys, sometimes just by hearing about them. ("Wait, Microsoft is selling a watch that requires a $10 monthly subscription, has to be recharged every other day and doesn't fully work outside your own area code? You're kidding, right?")

Smart companies should inspect the smoking wreckage of their predecessors' marketplace disasters and learn the factors at work. For example:

THE UPGRADE PARADOX. Both the hardware and software industries have adopted a business model in which a new version, with more features, is introduced each year. At the outset, this cycle works for everyone. We, the people, cheerfully upgrade every year just to stay current. The tech company captures repeat business. Ultimately, though, simply piling on new features impairs the product rather than enhancing it. As Apple's Steve Jobs has said, the real art is knowing what to leave out, not what to put in.

GOOD DESIGN ISN'T EASY. Our gadgets are under warring design constraints. We want our electronics tiny and pocketable, but we want big screens and keyboards. We want our devices rugged but also inexpensive. We want them powerful but with a long battery life, packed with features and easy to use. Finding a design that strikes just the right balance in all these areas is darned hard.

PRESSURE TO SHIP. Far more products fall behind schedule than surge ahead of it. Meanwhile the money people want to see a return on their investment. Eventually the pressure to ship the new product becomes intense—especially at the holiday season—even if everyone knows it's not quite finished. That's what happened to the disastrous BlackBerry Storm, the first touchscreen BlackBerry, whose original version was so buggy and half-baked that it became the laughingstock of the Web.

Tech companies seem to think it's okay to ship a poorly developed product, filled with bugs and bad design, and fix it later.

FIX IT LATER SYNDROME. Tech companies seem to think it's okay to ship a poorly developed product (especially software or a Web site), filled with bugs and bad design, and then fix it later. "It's only software," they say. "Let the first customers be our guinea pigs."

Which is fine—unless your product is so bad, it doesn't even make it to version 2. Beware the fate of *Remo Williams: The Adventure Begins,* a movie so bad, the adventure never even continued.

THE BROADWAY FLOP EFFECT. I spent 10 years working as a conductor and arranger of Broadway musicals, many of which were flops. (I hope that wasn't *because* I worked on them.) Everyone in the cast and crew was perfectly aware that we were working on a flop. But nobody ever spoke up. We all just showed up for work and did as we were told. Why? Because it was a paycheck. We would be idiots to suggest to the management that the emperor had no clothes.

Even if a tech project team knows that its product is a dog, there's no incentive for the rank and file to speak up—and plenty of incentive to keep heads down and see it through to its disappointing end.

So, yes, there are all kinds of factors that contribute to consumer tech turkeys. What is fascinating is how rarely the problem is the nature of the technology itself. Far more often the real problem is simple human nature. SA

THE ALL BUT FORGOTTEN FLOPS
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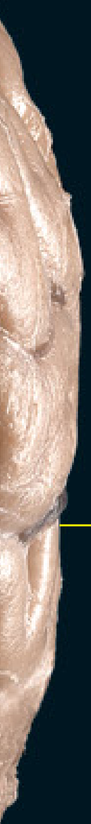


NEUROSCIENCE

The Limits of Intelligence

The laws of physics may well prevent the human brain from evolving into an ever more powerful thinking machine

By Douglas Fox

Photograph by Adam Voorhes

Douglas Fox is a freelance writer living in San Francisco. He is a frequent contributor to *New Scientist, Discover,* the *Christian Science Monitor* and a recipient of several awards, most recently of an Award for Reporting on a Significant Topic from the American Society of Journalists and Authors.

SANTIAGO RAMÓN Y CAJAL, THE SPANISH NOBEL-WINNING BIOLOGIST who mapped the neural anatomy of insects in the decades before World War I, likened the minute circuitry of their vision-processing neurons to an exquisite pocket watch. He likened that of mammals, by comparison, to a hollow-chested grandfather clock. Indeed, it is humbling to think that a honeybee, with its milligram-size brain, can perform tasks such as navigating mazes and landscapes on a par with mammals. A honeybee may be limited by having comparatively few neurons, but it surely seems to squeeze everything it can out of them.

At the other extreme, an elephant, with its five-million-fold larger brain, suffers the inefficiencies of a sprawling Mesopotamian empire. Signals take more than 100 times longer to travel between opposite sides of its brain—and also from its brain to its foot, forcing the beast to rely less on reflexes, to move more slowly, and to squander precious brain resources on planning each step.

We humans may not occupy the dimensional extremes of elephants or honeybees, but what few people realize is that the laws of physics place tough constraints on our mental faculties as well. Anthropologists have speculated about anatomic roadblocks to brain expansion—for instance, whether a larger brain could fit through the birth canal of a bipedal human. If we assume, though, that evolution can solve the birth canal problem, then we are led to the cusp of some even more profound questions.

One might think, for example, that evolutionary processes could increase the number of neurons in our brain or boost the rate at which those neurons exchange information and that such changes would make us smarter. But several recent trends of investigation, if taken together and followed to their logical conclusion, seem to suggest that such tweaks would soon run into physical limits. Ultimately those limits trace back to the very nature of neurons and the statistically noisy chemical exchanges by which they communicate. "Information, noise and energy are inextricably linked," says Simon Laughlin, a theoretical neuroscientist at the University of Cambridge. "That connection exists at the thermodynamic level."

Do the laws of thermodynamics, then, impose a limit on neuron-based intelligence, one that applies universally, whether in birds, primates, porpoises or praying mantises? This question apparently has never been asked in such broad terms, but the scientists interviewed for this article generally agree that it is a question worth contemplating. "It's a very interesting point," says Vijay Balasubramanian, a physicist who studies neural coding of information at the University of Pennsylvania. "I've never even seen this point discussed in science fiction."

Intelligence is of course a loaded word: it is hard to measure and even to define. Still, it seems fair to say that by most metrics, humans are the most intelligent animals on earth. But as our brain has evolved, has it approached a hard limit to its ability to process information? Could there be some physical limit to the evolution of neuron-based intelligence—and not just for humans but for all of life as we know it?

THAT HUNGRY TAPEWORM IN YOUR HEAD

THE MOST INTUITIVELY OBVIOUS WAY in which brains could get more powerful is by growing larger. And indeed, the possible connection between brain size and intelligence has fascinated scientists

IN BRIEF

Human intelligence may be close to its evolutionary limit. Various lines of research suggest that most of the tweaks that could make us smarter would hit limits set by the laws of physics.

Brain size, for instance, helps up to a point but carries diminishing returns: brains become energy-hungry and slow. Better "wiring" across the brain also would consume energy and take up a disproportionate amount of space.

Making wires thinner would hit thermodynamic limitations similar to those that affect transistors in computer chips: communication would get noisy.

Humans, however, might still achieve higher intelligence collectively. And technology, from writing to the Internet, enables us to expand our mind outside the confines of our body.

for more than 100 years. Biologists spent much of the late 19th century and the early 20th century exploring universal themes of life—mathematical laws related to body mass, and to brain mass in particular, that run across the animal kingdom. One advantage of size is that a larger brain can contain more neurons, which should enable it to grow in complexity as well. But it was clear even then that brain size alone did not determine intelligence: a cow carries a brain well over 100 times larger than a mouse's, but the cow isn't any smarter. Instead brains seem to expand with body size to carry out more trivial functions: bigger bodies might, for example, impose a larger workload of neural housekeeping chores unrelated to intelligence, such as monitoring more tactile nerves, processing signals from larger retinas and controlling more muscle fibers.

Eugene Dubois, the Dutch anatomist who discovered the skull of *Homo erectus* in Java in 1892, wanted a way to estimate the intelligence of animals based on the size of their fossil skulls, so he worked to define a precise mathematical relation between the brain size and body size of animals—under the assumption that animals with disproportionately large brains would also be smarter. Dubois and others amassed an ever growing database of brain and body weights; one classic treatise reported the body, organ and gland weights of 3,690 animals, from wood roaches to yellow-billed egrets to two-toed and three-toed sloths.

Dubois's successors found that mammals' brains expand more slowly than their bodies—to about the ¾ power of body mass. So a muskrat, with a body 16 times larger than a mouse's, has a brain about eight times as big. From that insight came the tool that Dubois had sought: the encephalization quotient, which compares a species' brain mass with what is predicted based on body mass. In other words, it indicates by what factor a species deviates from the ¾ power law. Humans have a quotient of 7.5 (our brain is 7.5 times larger than the law predicts); bottlenose dolphins sit at 5.3; monkeys hover as high as 4.8; and oxen—no surprise there—slink around at 0.5 [*see box at right*]. In short, intelligence may depend on the amount of neural reserve that is left over after the brain's menial chores, such as minding skin sensations, are accounted for. Or to boil it down even more: intelligence may depend on brain size in at least a superficial way.

As brains expanded in mammals and birds, they almost certainly benefited from economies of scale. For example, the greater number of neural pathways that any one signal between neurons can travel means that each signal implicitly carries more information, implying that the neurons in larger brains can get away with firing fewer times per second. Meanwhile, however, another, competing trend may have kicked in. "I think it is very likely that there is a law of diminishing returns" to increasing intelligence indefinitely by adding new brain cells, Balasubramanian says. Size carries burdens with it, the most obvious one being added energy consumption. In humans, the brain is already the hungriest part of our body: at 2 percent of our body weight, this greedy little tapeworm of an organ wolfs down 20 percent of the calories that we expend at rest. In newborns, it's an astounding 65 percent.

STAYING IN TOUCH

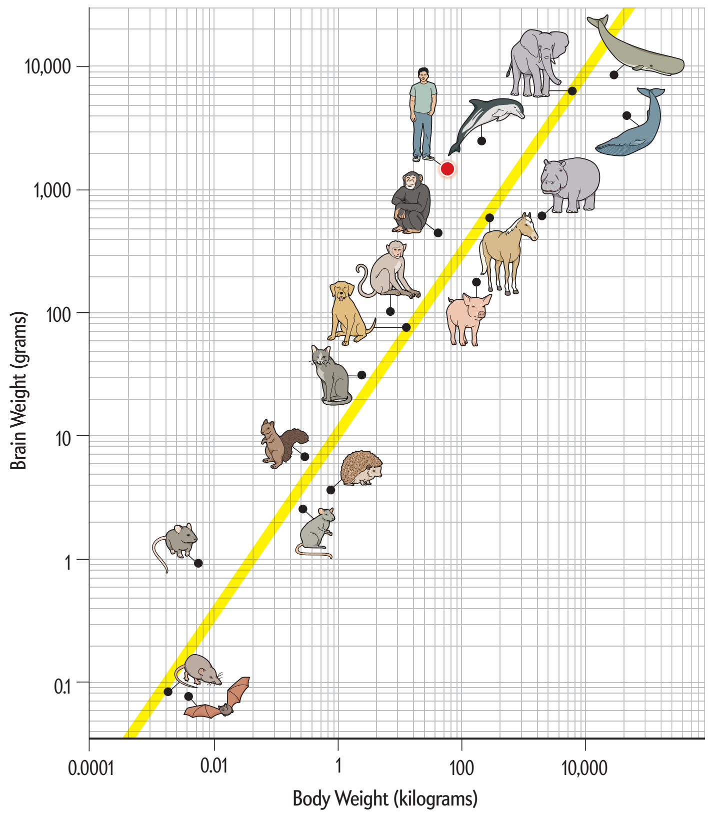
MUCH OF THE ENERGETIC BURDEN of brain size comes from the organ's communication networks: in the human cortex, communications account for 80 percent of energy consumption. But it appears that as size increases, neuronal connectivity also becomes more challenging for subtler, structural reasons. In fact, even as biologists kept collecting data on brain mass in the early to mid-20th century, they delved into a more daunting enterprise: to define the "design principles" of brains and how these principles are maintained across brains of different sizes.

A typical neuron has an elongated tail called the axon. At its end, the axon branches out, with the tips of the branches forming synapses, or contact points, with other cells. Axons, like telegraph

A SCALING LAW AND ITS EXCEPTIONS

Brain-Size Outliers

Whether they are smarter or not, larger animals typically have larger brains, although brain size grows not as a fixed percentage but as the ¾ power of body mass, a law that in the logarithmic scale below is represented by a straight line. Unusually smart animals, then, are those that deviate from this power law and place farther up than the line; humans beat the law by a factor of 7.5, the best of any species. Beyond a point, however, increasing brain size brings diminishing returns [*see box on page 42*].



SOURCE: "BRAIN SIZE IN VERTEBRATES" BY P.A.M. VAN DONGEN, IN *THE CENTRAL NERVOUS SYSTEM OF VERTEBRATES*, VOL. 3, EDITED BY R. NIEUWENHUYS ET AL., SPRINGER, 1998

Graphic by Brown Bird Design

wires, may connect different parts of the brain or may bundle up into nerves that extend from the central nervous system to the various parts of the body.

In their pioneering efforts, biologists measured the diameter of axons under microscopes and counted the size and density of nerve cells and the number of synapses per cell. They surveyed hundreds, sometimes thousands, of cells per brain in dozens of species. Eager to refine their mathematical curves by extending them to ever larger beasts, they even found ways to extract intact brains from whale carcasses. The five-hour process, meticulously described in the 1880s by biologist Gustav Adolf Guldberg, involved the use of a two-man lumberjack saw, an ax, a chisel and plenty of strength to open the top of the skull like a can of beans.

These studies revealed that as brains expand in size from species to species, several subtle but probably unsustainable changes happen. First, the average size of nerve cells increases. This phenomenon allows the neurons to connect to more and more of their compatriots as the overall number of neurons in the brain increases. But larger cells pack into the cerebral cortex less densely, so the distance between cells increases, as does the length of axons required to connect them. And because longer axons mean longer times for signals to travel between cells, these projections need to become thicker to maintain speed (thicker axons carry signals faster).

Researchers have also found that as brains get bigger from species to species, they are divided into a larger and larger number of distinct areas. You can see those areas if you stain brain tissue and view it under a microscope: patches of the cortex turn different colors. These areas often correspond with specialized functions, say, speech comprehension or face recognition. And as brains get larger, the specialization unfolds in another dimension: equivalent areas in the left and right hemispheres take on separate functions—for example, spatial versus verbal reasoning.

For decades this dividing of the brain into more work cubicles was viewed as a hallmark of intelligence. But it may also reflect a more mundane truth, says Mark Changizi, a theoretical neurobiologist at 2AI Labs in Boise, Idaho: specialization compensates for the connectivity problem that arises as brains get bigger. As you go from a mouse brain to a cow brain with 100 times as many neurons, it is impossible for neurons to expand quickly enough to stay just as well connected. Brains solve this problem by segregating like-functioned neurons into highly interconnected modules, with far fewer long-distance connections between modules. The specialization between right and left hemispheres solves a similar problem; it reduces the amount of information that must flow between the hemispheres, which minimizes the number of long, interhemispheric axons that the brain needs to maintain. "All of these seemingly complex things about bigger brains are just the backbends that the brain has to do to satisfy the connectivity problem" as it gets larger, Changizi argues. "It doesn't tell us that the brain is smarter."

Jan Karbowski, a computational neuroscientist at the Polish Academy of Sciences in Warsaw, agrees. "Somehow brains have to optimize several parameters simultaneously, and there must be trade-offs," he says. "If you want to improve one thing, you screw up something else." What happens, for example, if you expand the corpus callosum (the bundle of axons connecting right and left hemispheres) quickly enough to maintain constant connectivity as brains expand? And what if you thicken those axons, so the transit delay for signals traveling between hemispheres does not increase as brains expand? The results would not be pretty. The corpus callosum would expand—and push the hemispheres apart—so quickly that any performance improvements would be neutralized.

"Cortical gray matter neurons are working with axons that are pretty close to the physical limit."
—Simon Laughlin, *University of Cambridge*

These trade-offs have been laid into stark relief by experiments showing the relation between axon width and conduction speed. At the end of the day, Karbowski says, neurons do get larger as brain size increases, but not quite quickly enough to stay equally well connected. And axons do get thicker as brains expand, but not quickly enough to make up for the longer conduction delays.

Keeping axons from thickening too quickly saves not only space but energy as well, Balasubramanian says. Doubling the width of an axon doubles energy expenditure, while increasing the velocity of pulses by just 40 percent or so. Even with all of this corner cutting, the volume of white matter (the axons) still grows more quickly than the volume of gray matter (the main body of neurons containing the cell nucleus) as brains increase in size. To put it another way, as brains get bigger, more of their volume is devoted to wiring rather than to the parts of individual cells that do the actual computing, which again suggests that scaling size up is ultimately unsustainable.

THE PRIMACY OF PRIMATES

IT IS EASY, with this dire state of affairs, to see why a cow fails to squeeze any more smarts out of its grapefruit-size brain than a mouse does from its blueberry-size brain. But evolution has also achieved impressive workarounds at the level of the brain's building blocks. When Jon H. Kaas, a neuroscientist at Vanderbilt University, and his colleagues compared the morphology of brain cells across a spectrum of primates in 2007, they stumbled onto a game changer—one that has probably given humans an edge.

Kaas found that unlike in most other mammals, cortical neurons in primates enlarge very little as the brain increases in size. A few neurons do increase in size, and these rare ones may shoulder the burden of keeping things well connected. But the majority do not get larger. Thus, as primate brains expand from species to species, their neurons still pack together almost as densely. So from the marmoset to the owl monkey—a doubling in brain mass—the number of neurons roughly doubles, whereas in rodents with a similar doubling of mass the number of neurons increases by just 60 percent. That difference has huge consequences. Humans pack 100 billion neurons into 1.4 kilograms of brain, but a rodent that had followed its usual neuron-size scaling law to reach that number of neurons would now have to drag around a brain weighing 45 kilograms. And metabolically speaking, all that brain matter would eat the varmint out of house and home. "That may be one of the factors in why the large rodents don't seem to be [smarter] at all than the small rodents," Kaas says.

Having smaller, more densely packed neurons does seem to have a real impact on intelligence. In 2005 neurobiologists Gerhard Roth and Urusula Dicke, both at the University of Bremen in Germany, reviewed several traits that predict intelligence across species (as measured, roughly, by behavioral complexity) even more effectively than the encephalization quotient does. “The only tight correlation with intelligence,” Roth says, “is in the number of neurons in the cortex, plus the speed of neuronal activity,” which decreases with the distance between neurons and increases with the degree of myelination of axons. Myelin is fatty insulation that lets axons transmit signals more quickly.

If Roth is right, then primates’ small neurons have a double effect: first, they allow a greater increase in cortical cell number as brains enlarge; and second, they allow faster communication, because the cells pack more closely. Elephants and whales are reasonably smart, but their larger neurons and bigger brains lead to inefficiencies. “The packing density of neurons is much lower,” Roth says, “which means that the distance between neurons is larger and the velocity of nerve impulses is much lower.”

In fact, neuroscientists have recently seen a similar pattern in variations within humans: people with the quickest lines of communication between their brain areas also seem to be the brightest. One study, led in 2009 by Martijn P. van den Heuvel of the University Medical Center Utrecht in the Netherlands, used functional magnetic resonance imaging to measure how directly different brain areas talk to one another—that is, whether they talk via a large or a small number of intermediary areas. Van den Heuvel found that shorter paths between brain areas correlated with higher IQ. Edward Bullmore, an imaging neuroscientist at the University of Cambridge, and his collaborators obtained similar results the same year using a different approach. They compared working memory (the ability to hold several numbers in one’s memory at once) among 29 healthy people. They then used magnetoencephalographic recordings from their subjects’ scalp to estimate how quickly communication flowed between brain areas. People with the most direct communication and the fastest neural chatter had the best working memory.

It is a momentous insight. We know that as brains get larger, they save space and energy by limiting the number of direct connections between regions. The large human brain has relatively few of these long-distance connections. But Bullmore and van den Heuvel showed that these rare, nonstop connections

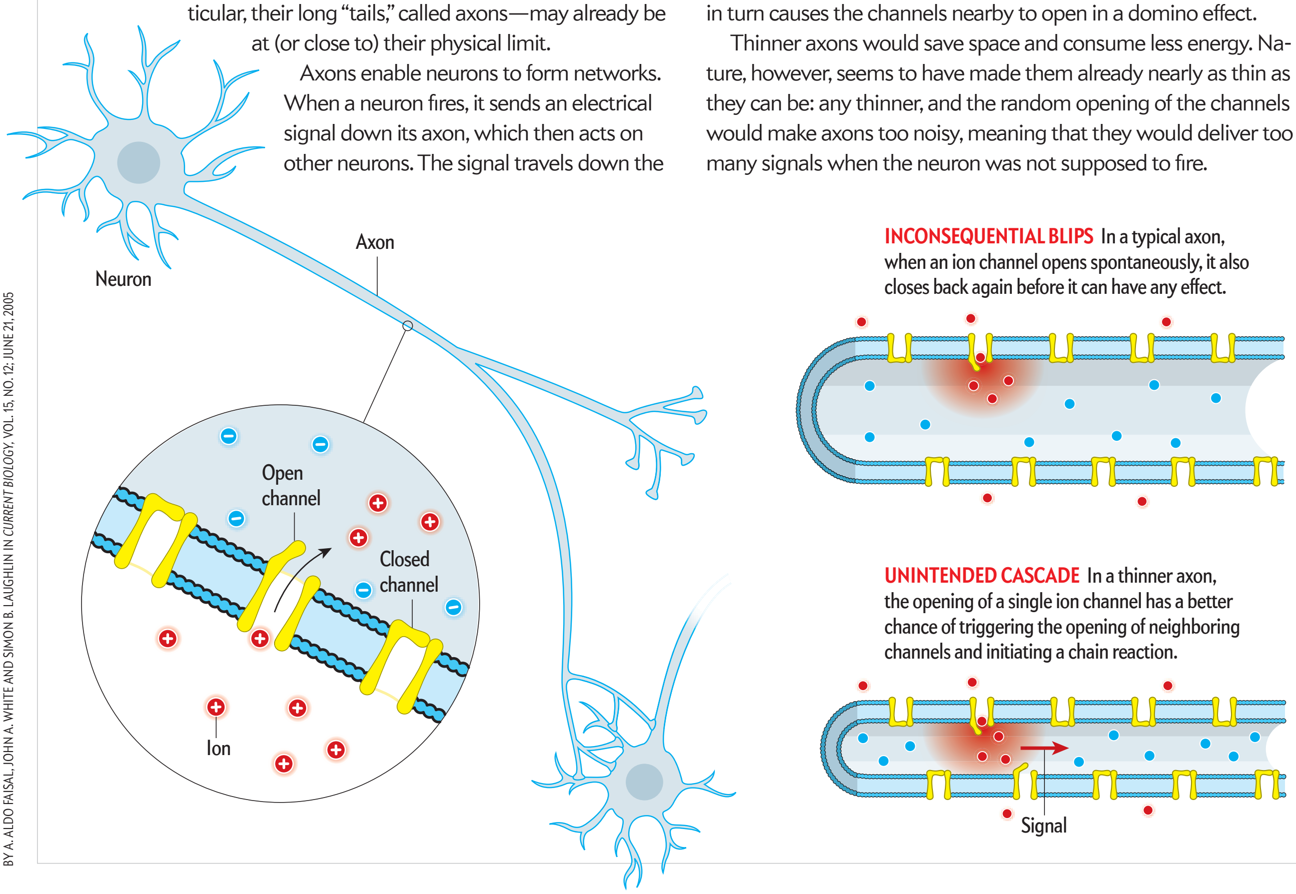
MINIATURIZATION HITS A LIMIT

The Physics of Thought

Just as shrinking transistors makes computers more powerful, brains with smaller components could, in principle, pack in more power and become faster. Human neurons, however—and in particular, their long “tails,” called axons—may already be at (or close to) their physical limit.

Axons enable neurons to form networks. When a neuron fires, it sends an electrical signal down its axon, which then acts on other neurons. The signal travels down the axon by opening ion channels embedded in the cellular membrane (*inset*), which let ions through. When enough ions cross a channel, they change the voltage across the membrane, which in turn causes the channels nearby to open in a domino effect.

Thinner axons would save space and consume less energy. Nature, however, seems to have made them already nearly as thin as they can be: any thinner, and the random opening of the channels would make axons too noisy, meaning that they would deliver too many signals when the neuron was not supposed to fire.



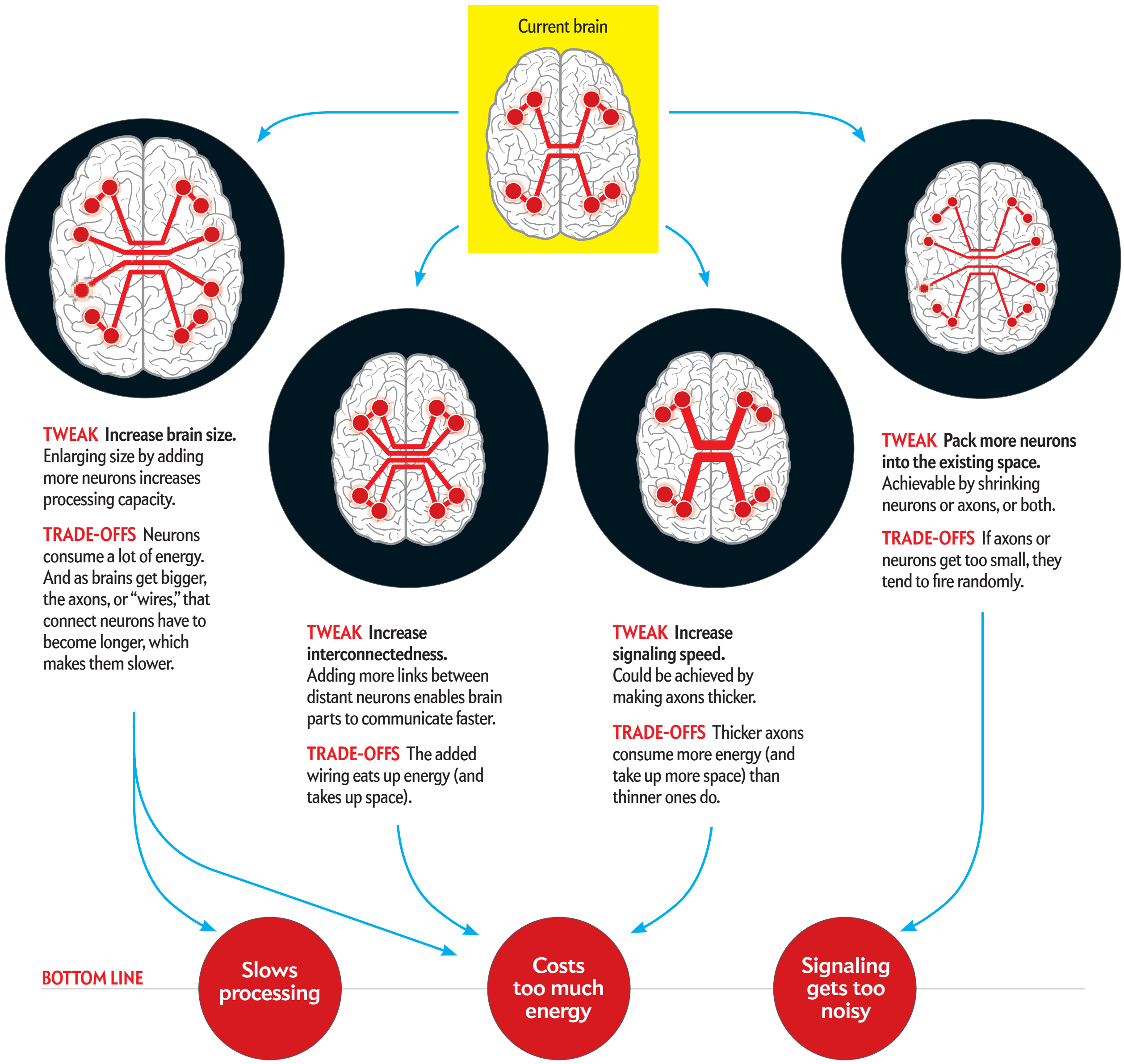
SOURCE: “ION-CHANNEL NOISE PLACES LIMITS ON THE MINIATURIZATION OF THE BRAIN’S WIRING,” BY A. ALDO FAISAL, JOHN A. WHITE AND SIMON B. LAUGHLIN IN *CURRENT BIOLOGY*, VOL. 15, NO. 12; JUNE 21, 2005

Illustration by Brown Bird Design

THE TRADE-OFF PROBLEM

Why We Probably Cannot Get Much Smarter

Miniaturization is just one of several evolutionary tweaks that could, in principle, enhance our intelligence and at the same time carry disadvantages and run into thermodynamic hurdles. Perhaps we are already close to being as smart as a neuron-based intelligence can be.



have a disproportionate influence on smarts: brains that scrimp on resources by cutting just a few of them do noticeably worse. "You pay a price for intelligence," Bullmore concludes, "and the price is that you can't simply minimize wiring."

INTELLIGENCE DESIGN

IF COMMUNICATION BETWEEN NEURONS, and between brain areas, is really a major bottleneck that limits intelligence, then evolving neurons that are even smaller (and closer together, with faster communication) should yield smarter brains. Similarly, brains might become more efficient by evolving axons that can carry signals faster over longer distances without getting thicker. But something prevents animals from shrinking neurons and axons beyond a certain point. You might call it the mother of all limitations: the proteins that neurons use to generate electrical pulses, called ion channels, are inherently unreliable.

Ion channels are tiny valves that open and close through changes in their molecular folding. When they open, they allow

Illustration by Brown Bird Design

ions of sodium, potassium or calcium to flow across cell membranes, producing the electrical signals by which neurons communicate. But being so minuscule, ion channels can get flipped open or closed by mere thermal vibrations. A simple biology experiment lays the defect bare. Isolate a single ion channel on the surface of a nerve cell using a microscopic glass tube, sort of like slipping a glass cup over a single ant on a sidewalk. When you adjust the voltage on the ion channel—a maneuver that causes it to open or close—the ion channel does not flip on and off reliably like your kitchen light does. Instead it flutters on and off randomly. Sometimes it does not open at all; other times it opens when it should not. By changing the voltage, all you do is change the *likelihood* that it opens.

It sounds like a horrible evolutionary design flaw—but in fact, it is a compromise. "If you make the spring on the channel too loose, then the noise keeps on switching it," Laughlin says—as happens in the biology experiment described earlier. "If you make the spring on the channel stronger, then you get less noise," he says, "but now it's more work to switch it," which forces neurons to spend more energy to control the ion channel. In other words, neurons save energy by using hair-trigger ion channels, but as a side effect the channels can flip open or close accidentally. The trade-off means that ion channels are reliable only if you use large numbers of them to "vote" on whether or not a neuron will generate an impulse. But voting becomes problematic as neurons get smaller. "When you reduce the size of neurons, you reduce the number of channels that are available to carry the signal," Laughlin says. "And that increases the noise."

In a pair of papers published in 2005 and 2007, Laughlin and his collaborators calculated whether the need to include enough ion channels limits how small axons can be made. The results were startling. "When axons got to be about 150 to 200 nanometers in diameter, they became impossibly noisy," Laughlin says. At that point, an axon contains so few ion channels that the accidental opening of a single channel can spur the axon to deliver a signal even though the neuron did not intend to fire [*see box on page 41*]. The brain's smallest axons probably already hiccup out about six of these accidental spikes per second. Shrink them just a little bit more, and they would blather out more than 100 per second. "Cortical gray matter neurons are working with axons that are pretty close to the physical limit," Laughlin concludes.

This fundamental compromise between information, energy and noise is not unique to biology. It applies to everything from optical-fiber communications to ham radios and computer chips. Transistors act as gatekeepers of electrical signals, just like ion channels do. For five decades engineers have shrunk transistors steadily, cramming more and more onto chips to produce ever faster computers. Transistors in the latest chips are 22 nanometers. At those sizes, it becomes very challenging to "dope" silicon uniformly (doping is the addition of small quantities of other elements to adjust a semiconductor's properties). By the time they reach about 10 nanometers, transistors will be so small that the random presence or absence of a single atom of boron will cause them to behave unpredictably.

Engineers might circumvent the limitations of current transistors by going back to the drawing board and redesigning chips to use entirely new technologies. But evolution cannot start from scratch: it has to work within the scheme and with the parts that have existed for half a billion years, explains Heinrich Reichert, a developmental neurobiologist at the University of Basel in Switzerland—like building a battleship with modified airplane parts.

Moreover, there is another reason to doubt that a major evolutionary leap could lead to smarter brains. Biology may have had a wide range of options when neurons first evolved, but 600 million years later a peculiar thing has happened. The brains of the honeybee, the octopus, the crow and intelligent mammals, Roth points out, look nothing alike at first glance. But if you look at the circuits that underlie tasks such as vision, smell, navigation and episodic memory of event sequences, "very astonishingly they all have absolutely the same basic arrangement." Such evolutionary convergence usually suggests that a certain anatomical or physiological solution has reached maturity so that there may be little room left for improvement.

Perhaps, then, life has arrived at an optimal neural blueprint. That blueprint is wired up through a step-by-step choreography in which cells in the growing embryo interact through signaling molecules and physical nudging, and it is evolutionarily entrenched.

BEES DO IT

SO HAVE HUMANS reached the physical limits of how complex our brain can be, given the building blocks that are available to us? Laughlin doubts that there is any hard limit on brain function the way there is one on the speed of light. "It's more likely you just have a law of diminishing returns," he says. "It becomes less and less worthwhile the more you invest in it." Our brain can pack in only so many neurons; our neurons can establish only so many connections among themselves; and those connections can carry only so many electrical impulses per second. Moreover, if our body and brain got much bigger, there would be costs in terms of energy consumption, dissipation of heat and the sheer time it takes for neural impulses to travel from one part of the brain to another.

The human mind, however, may have better ways of expanding without the need for further biological evolution. After all, honeybees and other social insects do it: acting in concert with their hive sisters, they form a collective entity that is smarter than the sum of its parts. Through social interaction we, too, have learned to pool our intelligence with others.

And then there is technology. For millennia written language has enabled us to store information outside our body, beyond the capacity of our brain to memorize. One could argue that the Internet is the ultimate consequence of this trend toward outward expansion of intelligence beyond our body. In a sense, it could be true, as some say, that the Internet makes you stupid: collective human intelligence—culture and computers—may have reduced the impetus for evolving greater individual smarts. SA

MORE TO EXPLORE

Evolution of the Brain and Intelligence. Gerhard Roth and Ursula Dicke in *Trends in Cognitive Sciences,* Vol. 9, No. 5, pages 250–257; May 2005.

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Efficiency of Functional Brain Networks and Intellectual Performance. Martijn P. van den Heuvel, Cornelis J. Stam, René S. Kahn and Hilleke E. Hulshoff Pol in *Journal of Neuroscience,* Vol. 29, No. 23, pages 7619–7624; June 10, 2009.

SCIENTIFIC AMERICAN ONLINE
Hear an interview with the author at **ScientificAmerican.com/jul2011/brain**

Pleiades star cluster, one of the best known and studied, is so young that many of its massive, blue, short-lived stars are still shining. The cluster was the subject of the first published "periodic table" of astronomy, which became known as the Hertzsprung-Russell diagram.

ROGELIO BERNAL ANDREO *deepskycolors.com*

ASTROPHYSICS

THE PERIODIC TABLE OF THE COSMOS

A simple diagram, which celebrates its centennial this year, continues to serve as the most essential conceptual tool in stellar astrophysics

By Ken Croswell

MODERN ASTRONOMY PAINTS A VIVID PICTURE OF the universe having been born in a cataclysmic bang and filled with exotic stars ranging from gargantuan red supergiants that span the size of a modest solar system to hyperdense white dwarf stars and black holes that are smaller than Earth. These discoveries are all the more remarkable because astronomers infer them from the faintest glimmers of light, sometimes just a handful of photons. A key to this suc-

Continued on page 48

A USER'S GUIDE TO THE H-R DIAGRAM

STELLAR COLOR AND TYPE

The color of a star reflects the temperature of its surface, from tepid red-hot (*far right*) to sizzling blue-hot (*far left*). Astronomers divide stars into seven main spectral types, based on which chemical elements in their outer layers absorb light, which in turn depends on temperature: O, B, A, F, G, K and M. The universal mnemonic is "*Oh, be a fine girl/guy, kiss me!*" although the alternative "*Oh, boy, an F grade kills me!*" has its appeal.

MAIN SEQUENCE

Most stars fall in a diagonal line, indicating that their luminosity and temperature are determined by a third, even more basic property: mass. The hot, bright stars on the left are the most massive. Once a star begins producing energy by fusing hydrogen nuclei, it achieves a stable internal equilibrium and stays near the same spot on the diagram for most of its life.

GIANTS/SUPERGIANTS

These are ex-main-sequence stars that have exhausted the hydrogen in their core and now devour other reservoirs of fuel, such as helium. The most massive become supergiants; lesser ones, giants. If a large red supergiant replaced the sun, it would engulf all the planets out to Jupiter. These stars do not remain at a fixed position on the diagram but move around as they age.

HYPERGIANTS

The most massive stars of all are found near the top of the diagram. The current record holder is R136a1, which, at birth, was 320 times as massive as the sun; since then, it has lost mass by expelling gas. A similarly massive and unstable star is Eta Carinae, which is enveloped in a gaseous nebula from an outburst 170 years ago.

WHITE DWARFS

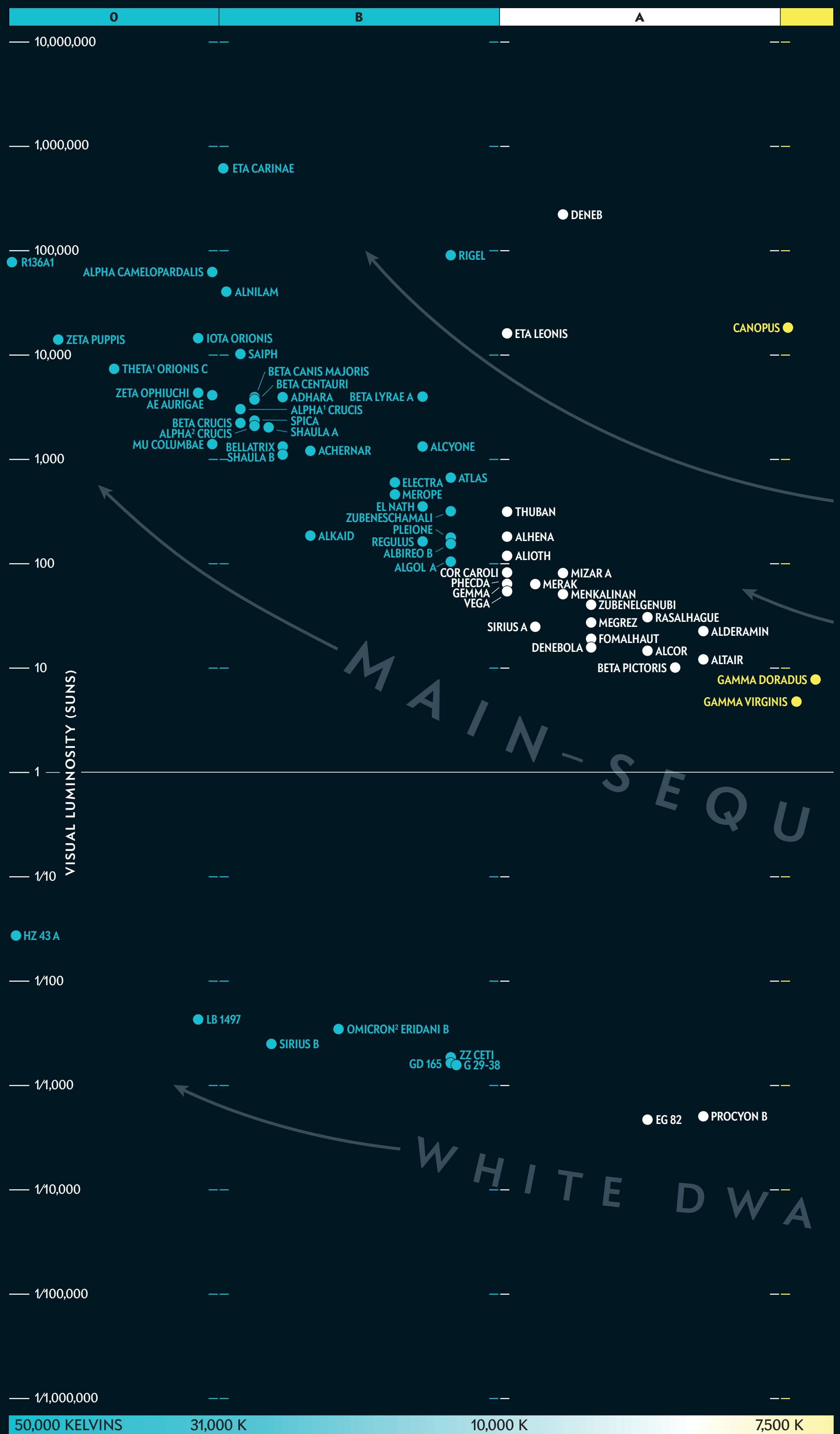
White dwarfs are stellar corpses. Unable to generate energy anymore, they pack themselves into balls barely the size of Earth. Their name notwithstanding, they span a range of colors. Over time a white dwarf slips down the chart to the right, until it can barely be seen.

SUN

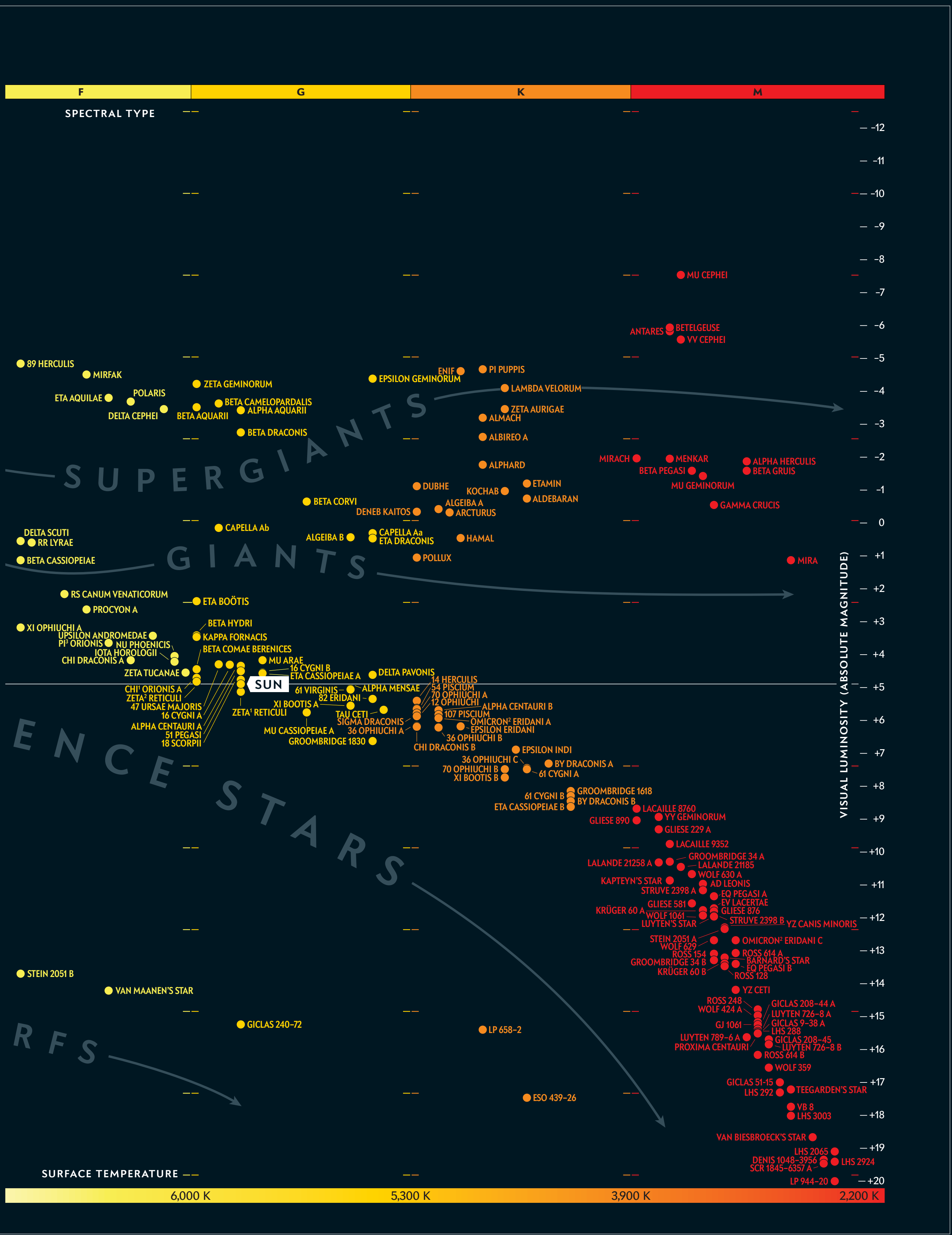
The sun lies on the main sequence. It came into being as a cool protostar and, once it exhausts its core's hydrogen fuel, will become a red giant and finally a white dwarf. Contrary to popular belief, the sun is not an average star; some 95 percent of stars lie below it in the diagram.

BROWN DWARFS

A frontier of astronomy is the detection and study of brown dwarfs, which are stars too light to undergo sustained nuclear fusion. On the diagram, they overlap with the dimmest, reddest stars at the bottom right and continue off the page to the right. (LP 944-20 is one.) A decade ago astronomers added spectral types L and T (*not shown*) to categorize them.



Graphic by Pitch Interactive, Stellar data from Ken Croswell



F
G
K
M
SPECTRAL TYPE
SUPERGIANTS
GIANTS
MAIN SEQUENCE STARS
DWARFS
VISUAL LUMINOSITY (ABSOLUTE MAGNITUDE)
–12
–11
–10
–9
–8
–7
–6
–5
–4
–3
–2
–1
0
+1
+2
+3
+4
+5
+6
+7
+8
+9
+10
+11
+12
+13
+14
+15
+16
+17
+18
+19
+20
MU CEPHEI
ANTARES
BETELGEUSE
VV CEPHEI
89 HERCULIS
MIRFAK
ENIF
PI PUPPIS
EPSILON GEMINORUM
ZETA GEMINORUM
LAMBDA VELORUM
POLARIS
ETA AQUILAE
BETA CAMELOPARDALIS
ALPHA AQUARII
ZETA AURIGAE
DELTA CEPHEI
BETA AQUARII
ALMACH
BETA DRACONIS
ALBIREO A
ALPHARD
MIRACH
MENKAR
ALPHA HERCULIS
BETA PEGASI
BETA GRUIS
MU GEMINORUM
ETAMIN
DUBHE
KOCHAB
ALDEBARAN
BETA CORVI
ALGEIBA A
DENEB KAITOS
ARCTURUS
GAMMA CRUCIS
CAPELLA Ab
DELTA SCUTI
RR LYRAE
ALGEIBA B
CAPELLA Aa
ETA DRACONIS
HAMAL
BETA CASSIOPEIAE
POLLUX
MIRA
RS CANUM VENATICORUM
ETA BOÖTIS
PROCYON A
BETA HYDRI
XI OPHIUCHI A
UPSILON ANDROMEDAE
KAPPA FORNACIS
PI³ ORIONIS
NU PHOENICIS
BETA COMAE BERENICES
IOTA HOROLOGII
CHI DRACONIS A
MU ARAE
16 CYGNI B
ZETA TUCANAE
ETA CASSIOPEIAE A
DELTA PAVONIS
14 HERCULIS
SUN
CHI¹ ORIONIS A
61 VIRGINIS
ALPHA MENSAE
54 PISCIUM
70 OPHIUCHI A
ZETA² RETICULI
82 ERIDANI
12 OPHIUCHI
47 URSAE MAJORIS
XI BOOTIS A
ALPHA CENTAURI B
16 CYGNI A
ZETA¹ RETICULI
TAU CETI
107 PISCIUM
SIGMA DRACONIS
OMICRON² ERIDANI A
ALPHA CENTAURI A
MU CASSIOPEIAE A
36 OPHIUCHI A
EPSILON ERIDANI
51 PEGASI
36 OPHIUCHI B
18 SCORPII
GROOMBRIDGE 1830
CHI DRACONIS B
EPSILON INDI
36 OPHIUCHI C
BY DRACONIS A
70 OPHIUCHI B
61 CYGNI A
XI BOOTIS B
GROOMBRIDGE 1618
61 CYGNI B
BY DRACONIS B
ETA CASSIOPEIAE B
LACAILLE 8760
GLIESE 890
YY GEMINORUM
GLIESE 229 A
LACAILLE 9352
GROOMBRIDGE 34 A
LALANDE 21258 A
LALANDE 21185
WOLF 630 A
KAPTEYN'S STAR
AD LEONIS
STRUVE 2398 A
EQ PEGASI A
EV LACERTAE
GLIESE 581
KRÜGER 60 A
GLIESE 876
WOLF 1061
STRUVE 2398 B
LUYTEN'S STAR
YZ CANIS MINORIS
STEIN 2051 A
OMICRON² ERIDANI C
WOLF 629
ROSS 154
ROSS 614 A
GROOMBRIDGE 34 B
BARNARD'S STAR
KRÜGER 60 B
EQ PEGASI B
ROSS 128
STEIN 2051 B
VAN MAANEN'S STAR
YZ CETI
ROSS 248
GICLAS 208–44 A
WOLF 424 A
LUYTEN 726–8 A
GICLAS 240–72
GJ 1061
GICLAS 9–38 A
LP 658–2
LHS 288
LUYTEN 789–6 A
GICLAS 208–45
PROXIMA CENTAURI
LUYTEN 726–8 B
ROSS 614 B
WOLF 359
GICLAS 51–15
LHS 292
TEEGARDEN'S STAR
ESO 439–26
VB 8
LHS 3003
VAN BIESBROECK'S STAR
LHS 2065
DENIS 1048–3956
LHS 2924
SCR 1845–6357 A
LP 944–20
SURFACE TEMPERATURE
6,000 K
5,300 K
3,900 K
2,200 K

Continued from page 45

cess is a graph that two astronomers introduced 100 years ago.

The Hertzsprung-Russell (H-R) diagram is simple. It plots two basic properties of stars: their luminosity (intrinsic brightness) and their surface temperature (as revealed by their color). In doing so, it anchors stellar astronomy just as the periodic table anchors chemistry. Whereas the periodic table groups together similar chemical elements—for example, placing all noble gases, such as helium, neon and argon, into one column—the H-R diagram groups together stars passing through similar stages of life. When astronomers invented the diagram, no one knew why the sun and other stars shine. No one knew how stars are born or how they die. No one could even assure the public that the sun would never explode. Nor did anyone know that the stars had forged most of the elements that make up Earth and our bodies.

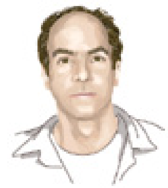
Not only did the diagram play a major role in solving these problems, it also guides astronomers today as they tackle key questions about the stars. How massive can a star be? What were the first stars to arise after the big bang? When will we see the next supernova in our galaxy?

A TOUR OF THE STELLAR BESTIARY

"NOBODY IMAGINED that I should become an astronomer," said Danish scientist Ejnar Hertzsprung. Indeed, when he was 20, his family sold his late father's astronomy books. Nevertheless, Hertzsprung persevered. He sketched his first luminosity-color diagram of star clusters in 1908. German astronomer Hans Rosenberg, who likely knew of Hertzsprung's work, published such a diagram in 1910, and Hertzsprung himself published several in 1911. At the time, he was an unknown. In contrast, Henry Norris Russell was one of America's foremost astronomers. In 1913, unaware of Hertzsprung's work, he plotted his own diagram. Because of Russell's prestige, astronomers first called the plot the Russell diagram, then the Russell-Hertzsprung diagram and finally—getting the historical order right—the Hertzsprung-Russell diagram.

As astronomers plotted stars on the graph, they discovered clear patterns. The vast majority, including the sun, lie on a diagonal line stretching from the upper left (bright and hot stars) to the lower right (dim and cool ones) [*see box on preceding two pages*]. This diagonal, which astronomers call the main sequence, is a startling revelation, because it links stars that seem to be opposites. Every main-sequence star generates light the same way: nuclear reactions convert hydrogen into helium at the star's center. The more mass a main-sequence star has, the hotter its center gets and the faster the reactions proceed, making the star brighter and hotter. Thus, the main sequence is really a mass sequence.

Ken Croswell, who earned a Ph.D. in astronomy at Harvard University for his study of stars in the Milky Way's halo, is an astronomer and author. His book *The Alchemy of the Heavens* (Anchor, 1995) was a Los Angeles Times Book Prize finalist. Croswell owes his interest in astronomy to his first grade teacher, who introduced him to the planets by instructing his class to make a map of the solar system.



Another stellar group appears above and to the right of the main sequence. It consists of stars that are brighter than main-sequence stars of the same temperature and color. Most are cooler than the sun; all are brighter. At first that sounds like a contradiction: the cooler a star is, the less light every square inch of its surface radiates, so how can a cool red star shine 100 or even 10,000 times more brightly than the sun? The answer is that these stars must be enormous—astronomers call them giants and supergiants. They are what main-sequence stars become after they exhaust the hydrogen fuel at their centers. Supergiants eventually explode as supernovae. Giants exit the scene more quietly.

In fact, the H-R diagram reveals the fate of the giants. The diagram contains a group of stars that form a diagonal line below the main sequence, which means they are dimmer than main-sequence stars of the same temperature and color. By the same reasoning as discussed, these stars must be tiny—astronomers call them white dwarfs. Despite their name, they stretch across many colors. They are the dense and intensely hot cores left behind when giants cast off their outer atmospheres. No longer capable of nuclear reactions, they usually cool and fade with time. If they are part of a binary star system, however, they can suck in matter from their companion star, reach a critical mass and go supernova.

The distinctive and ubiquitous patterns of the H-R diagram even reveal stellar properties that the diagram does not directly display. For example, astronomers can ascertain the age of a star cluster by plotting an H-R diagram just for the stars in that cluster. In the Pleiades cluster, for example, the main sequence extends to bright blue stars, whereas in the Hyades, such stars are missing. Consequently, the Hyades must be older; the bright blue stars it used to contain have all died off.

BIGGER AND BADDER

THE H-R DIAGRAM remains a vital tool. Much of today's research in stellar astronomy can be thought of as a way to explore the extremes of the diagram. At the bottom right are the dimmest, reddest, least massive stars. The main sequence ends with dim red stars that have about 8 percent of the sun's mass. Beyond is

IN BRIEF

Astronomy is remarkable for how it gleans so much knowledge from such meager slivers of light. A graph known as the Hertzsprung-Russell diagram, which marks its centennial this year, is part of the secret.

The diagram plots the luminosity and temperature of stars. On it, striking patterns emerge, classifying stars by their stage of life and revealing that most of their properties are ultimately determined by mass.

These patterns helped astronomers deduce that most stars, including the sun, shine by nuclear fusion reactions. They still guide research on stars today.

the realm of brown dwarfs, stars that are too lightweight to sustain nuclear fusion. Their properties and genesis still puzzle astronomers [see "The Mystery of Brown Dwarf Origins," by Subhanjoy Mohanty and Ray Jayawardhana; Scientific American, January 2006].

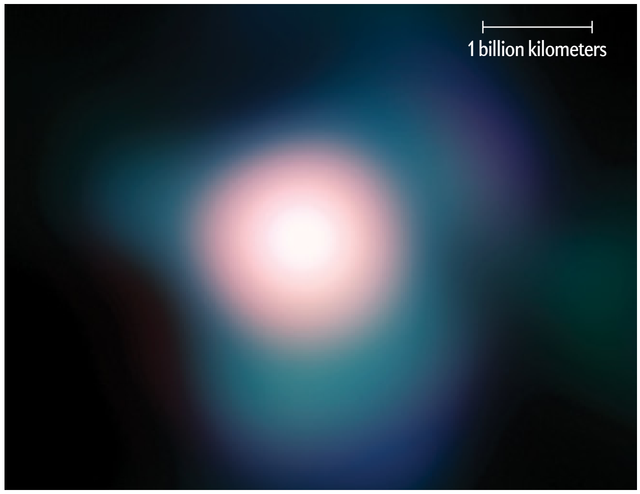
At the other end, the upper left of the H-R diagram is the home of the brightest, hottest, most massive main-sequence stars. But how massive can they get? Bright stars are easy to see but difficult to study because they are rare. Few are born, and those few burn their fuel so fast that they explode a few million years after birth. Studies of very young star clusters suggest that stars top out at about 150 times the sun's mass. Last year, however, Paul Crowther of the University of Sheffield in England and his colleagues upped the ante. They claimed that a star in the Large Magellanic Cloud, a modest nearby galaxy, was so bright and blue that it must have been born with a whopping 320 solar masses. Some astronomers are skeptical about the mass estimate, however, because it assumes that the star follows the same pattern of mass, brightness and temperature as ordinary main-sequence stars.

Whatever the case, the very first stars in the universe may have been even larger. The big bang created the three lightest elements: hydrogen, helium and a little lithium. The primordial soup lacked carbon and oxygen, which emit infrared light that escapes present-day interstellar clouds and thereby allows them to cool and fragment. Thus, the first star-forming gas clouds may have been warm and large, and they should have given birth to stars with hundreds of times the mass of the sun [see "The First Stars in the Universe," by Richard B. Larson and Volker Bromm; Scientific American, December 2001]. If so, they were much brighter and hotter than the most extreme stars today; they would therefore appear above and to the left of the upper left corner of the modern H-R diagram.

Any star born with more than eight times the mass of the sun someday explodes [see "How to Blow Up a Star," by Wolfgang Hillebrandt, Hans-Thomas Janka and Ewald Müller; Scientific American, October 2006]. Every year astronomers witness hundreds of supernova explosions in galaxies beyond our own. But not since 1604—before astronomers were using the telescope—have they witnessed a star go supernova in our galaxy. Which will be the next to self-destruct, and when will we see it?

The Milky Way spawns a couple of supernovae a century. But when one goes off, there is no guarantee we will see it. The Milky Way is vast—far larger than most other galaxies—and its disk is choked with interstellar dust, which blocks the light even of a supernova. Indeed, more than half a century ago astronomers discovered a giant cloud of debris named Cassiopeia A; the light from the explosion that created it reached Earth in the late 1600s but went unnoticed.

Thus, any exploding massive star that makes a splash in the sky will have to be nearby, probably within about 20,000 light-years of Earth. To find stars on the brink, astronomers look in the upper right of the H-R diagram—the realm of the red supergiants. The nearest and brightest are Betelgeuse and Antares, which are 640 and 550 light-years from Earth, respectively—close enough that their explosions will rival the moon in brightness but far enough that they should not hurt us.



Supergiant star Betelgeuse is one of only a handful of stars that astronomers can see as a disk rather than a mere point of light. This near-infrared image was taken by the European Southern Observatory's Very Large Telescope.

P. KERVELLA ESO

But the cosmos can always surprise us. The famous 1987 supernova in the Large Magellanic Cloud came not from a red supergiant but from a blue one. Similar stars also reside in our galaxy; they include two of the most conspicuous stars in the night sky, Deneb and Rigel.

Or we could see another type of supernova, which results when a white dwarf exceeds a critical mass. Although such supernovae are rarer, they are also more luminous and usually occur above or below the dusty disk, making them easier to see. Of the five supernovae in our galaxy astronomers have seen since A.D. 1000, three—and possibly four—were exploding white dwarfs. Unfortunately, white dwarfs are so dim that the suspects for triggering the next supernovae are not obvious.

Nevertheless, light from the next Milky Way supernova is racing toward us right now. When it finally arrives, astronomers will plot the progenitor's position on the H-R diagram to understand its life and death. Hertzsprung and Russell would be pleased to know that their creation still yields so much insight. Moreover, its success has inspired similar plots of other phenomena, notably, the many planets orbiting other stars. Such a graph may unveil as much about Earth's galactic relations as the H-R diagram has revealed about the sun's. SA

MORE TO EXPLORE

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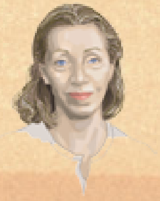
SCIENTIFIC AMERICAN ONLINE
Red star, blue star, big star, small star: The zoo of stars in the galaxy looks like something out of Dr. Seuss. Take a tour of it at **ScientificAmerican.com/jul2011/croswell**



Sharon Begley enjoys making sense of complex topics in neuroscience, genetics, psychology and health care. She has covered science for *Newsweek* and the *Wall Street Journal*.

HEALTH CARE

The *Best* Medicine

A quiet revolution in comparative effectiveness research just might save us from soaring medical costs

By Sharon Begley

IT WAS THE LARGEST AND MOST IMPORTANT INVESTIGATION of treatments for high blood pressure ever conducted, with a monumental price tag to match. U.S. doctors enrolled 42,418 patients from 623 offices and clinics, treated participants with one of four commonly prescribed drugs, and followed them for at least five years to see how well the medications controlled their blood pressure and reduced the risk of heart attack, stroke and other cardiovascular problems. It met the highest standards of medical research: neither physicians nor their patients knew who was placed in which treatment group, and patients had an equal chance of being assigned to any of the groups. Such randomized controlled trials have long been unmatched as a way to determine the safety and efficacy of drugs and other treatments. This one, dubbed ALLHAT (Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial), cost an estimated $120 million and took eight years to complete.

The results, announced in December 2002, were stunning: the oldest and cheapest of the drugs, known as thiazide-type diuretics, were more effective at reducing hypertension than the newer, more expensive ones. Furthermore, the diuretics, which work by ridding the body of excess fluid, were better at reducing the risk of developing heart failure, of being hospitalized and of having a stroke. ALLHAT was well worth its premium cost, argued the National Heart, Lung, and Blood Institute (NHLBI), which ran the trial. If patients were prescribed diuretics for hypertension rather than the more expensive medications, the nation would save $3.1 billion every decade in prescription drug costs alone—and hundreds of millions of dollars

Illustration by Alex Nabaum

more by avoiding stroke treatment, coronary artery bypass surgery and other consequences of high blood pressure.

But what should patients do if their blood pressure was not controlled by a diuretic alone, as happened with 60 percent of the ALLHAT patients? Which drugs should they turn to then? That was the next logical study to do, but the NHLBI could not afford to conduct another randomized controlled trial to find out. That is when David J. Magid had his big idea. As director of research for the Colorado Permanente Medical Group, part of the giant Kaiser Permanente health care organization, Magid had as much respect for classical clinical trials as the next scientist. But he thought there was a way to obtain equally rigorous results without going through the prolonged length and expense of a trial. Instead, he thought, he could comb through the thousands of electronic health records in Kaiser's database to find out which antihypertension drugs work best if diuretics do not bring about the needed reduction in blood pressure.

Magid had his answer in a year and a half, at a cost of only $200,000—a tiny fraction of the expected cost of a clinical trial. Two other heart medications, called angiotensin-converting enzyme (ACE) inhibitors and beta blockers, did an equally effective job as second-line treatments, he and his colleagues reported in 2010. Doctors could prescribe either drug to patients whose blood pressure was not controlled by a diuretic alone. "Randomized trials are so expensive and time-consuming, there's no way we can do them for all the important questions that need answering," Magid says. "Using health records [to compare treatments] offers a practical alternative."

DIFFICULT TRUTHS

MAGID IS A PIONEER in an increasingly influential movement to change the way clinicians and researchers determine which medications, surgeries or other treatments work best for a given illness or disorder. Formally called comparative effectiveness research (CER), it determines scientifically which therapies work and which do not. The approach is often easiest to understand in direct comparisons between different medications or between medication and surgery. But its methods are being used to evaluate a widening range of interventions, many of which have little to do with drugs—such as whether community health programs that offer transportation and housing assistance are more effective at keeping frail elderly men and women out of the hospital than programs that focus on more traditional medical services.

The need for greater scrutiny stems from pressing medical and economic challenges. The medical need for CER arises from a fact that few patients realize and fewer doctors acknowledge: the scientific basis for many medical treatments is often flimsy or even nonexistent. More than half the guidelines issued by the Infectious Disease Society of America, for instance, are based on "expert opinion" alone and not on actual comparative data, let alone a clinical trial. "There is a chasm between what gets done in practice and what science has shown," says Elizabeth A. McGlynn, the new director of Kaiser's Center for Effectiveness & Safety Research. At the same time, she notes, clinicians complain that scientific studies often cannot easily be translated to a real-world environment.

The economic imperative for comparative effectiveness research is just as compelling. Individual health plans have compared costs and outcomes of various treatments for years in an effort to trim their budgets, and yet health care spending in the U.S. has been projected to reach $2.7 trillion in 2011. That amount may sound like a reasonable price to pay for something consumers value (even if it dwarfs other expenditures, such as the $671 billion that will be spent by the Pentagon next year). Unnecessary health care spending, however, means that fewer dollars are available for investment, for education, for research and for other national needs. "As much as one third of our [medical] spending is for ineffective or unnecessary care," McGlynn says—around $900 billion a year, in other words. (By comparison, malpractice reform could save about $54 billion over 10 years, according to a 2009 analysis by the Congressional Budget Office.) "We can't afford to spend money on things that don't work," she continues, especially when the nation's soaring health care bills threaten to capsize state and local governments, businesses and Medicare, which are the "third parties" that pay for most of these medical costs. In an effort to save money by ensuring that the nation pays only for treatments that work, the economic stimulus bill of 2009 allocated $1.1 billion for comparative effectiveness research.

That is a lot of money but a pittance compared with the cost of such research—at least the traditional kind of CER, which uses clinical trials to distinguish therapies that help patients from those that do not—and how much of it is needed. A 2009 report by the Institute of Medicine, part of the National Academies, easily identified 100 questions of relative effectiveness that need answering. Multiplying 100 questions by a few hundred million dollars per question equals "unaffordable." Hence, the need for the novel, less costly approach to comparative effectiveness research such as Magid's, which exploits the latest information technology tools—from mining the databases of large, integrated health networks such as Kaiser's to sophisticated mathematical modeling of disease—in an effort to discover what works at a fraction of the cost of randomized controlled trials.

The cost of clinical trials is not the only impetus for the sea change under way in CER. The new research promises to yield better information: data that are more useful in clinical practice than data from traditional trials.

The reason is that clinical trials tend to enroll people who are younger, healthier and more likely to take prescribed medications; the study subjects are also monitored more closely by a

IN BRIEF

Soaring bill: U.S. health care costs are expected to top $2.7 trillion in 2011 and are growing at an unsustainable rate. One way to save money is to pay only for the most effective treatments.

Roadblock: Proving which treatments work best can be expensive and time-consuming. Randomized controlled trials, the most scientifically rigorous, often require hundreds of millions of dollars.

Sensible solution: Analyzing information found in the medical records of large health networks could reveal which treatments are most effective at a fraction of the cost of standard clinical trials.

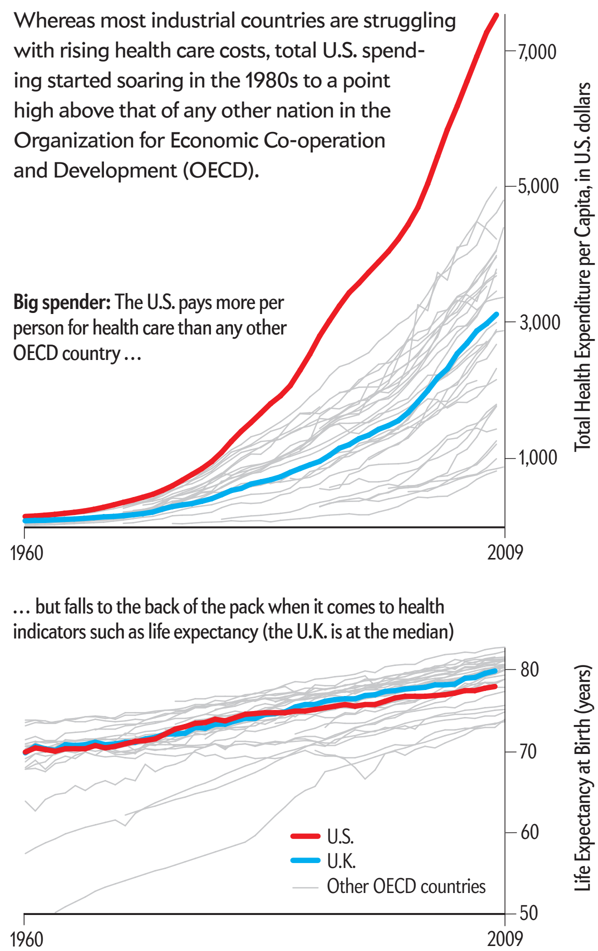
Political reality: Many Americans fear that talk about cost-cutting in health care will lead to rationing. But who wants to spend money on something that does not work?

physician than the average patient is. Some physicians therefore object that trial results may not apply to the older, sicker, less compliant patients they treat. In addition, traditional randomized clinical trials assess efficacy, which is the best-case, often idealized measure of a drug's or other therapy's benefits. In contrast, most physicians are concerned with effectiveness, which means how well a treatment works in real patients in real-world conditions. As a result, doctors can and do dismiss results obtained in the hothouse of randomized clinical trials as inapplicable to their patients. Despite ALLHAT, for instance, only 36 percent of first prescriptions for hypertension are diuretics, a 2009 study found, reflecting, in part, the belief of some physicians that the results are not relevant to their patients. If rigorous studies evaluate the real-world effectiveness of different interventions, Magid argues, more physicians would likely incorporate the results into their clinical practice.

As with any major changes to how health care is delivered in the U.S., CER is viewed with alarm by critics who are nervous that it might restrict physician autonomy and patient choice. But as the field develops rigorous, efficient ways to answer the most important question any patient or doctor can ask—what works?—it will inevitably play a growing and crucial role in health care at both the individual and policy level.

GLOBAL CONTEXT

Are We Getting Our Money's Worth?



SOURCE: OECD HEALTH DATA, 2010

INTO THE DATA MINE

FORTUNATELY, the need to find inexpensive ways to conduct comparative effectiveness research and get results relevant to real patients in the real world has coincided with another tectonic change in health care: the spread of electronic medical records. Kaiser Permanente has them on 8.6 million people. A new consortium of six medical institutions, including the Cleveland Clinic and the Mayo Clinic, has electronic records on 10 million. The Veterans Administration, a pioneer in electronic health records, as well as CER, cares for more than six million veterans annually. Crucially, in every case the medical institution's records are more complete and therefore more useful than standard Medicare claims data, which are often missing crucial details about a patient. All three—Kaiser, the consortium and the VA—have launched programs to mine those records by, for instance, taking all patients with type 2 diabetes, determining what treatment they got and comparing outcomes. "With these large databases and detailed clinical information, we can conduct comparative effectiveness research in real-world settings, with a full range of patients, not just those selected for clinical trials," says Joe V. Selby, director of Kaiser's division of research.

Analyzing millions of patients rather than the hundreds or thousands in a standard clinical trial also means the results are potentially more statistically sound—that is, findings are less likely to be to the result of chance. Another advantage of mining patient records: they include children and women of reproductive age, who are often barred from clinical trials because the risks are thought to outweigh the benefits.

At first glance, mining databases for information may seem a lot like conducting an old-style observational study, in which researchers find one group of patients who just happen to be receiving a particular therapy and another group who are receiving either no therapy or a different one. In contrast, a randomized controlled trial *assigns* patients to receive one or another treatment. Observational studies have yielded huge public health benefits (showing that cigarettes can cause lung cancer, for instance), but they can also mislead. It was observational studies that concluded, for instance, that long-term hormone therapy in older women whose estrogen levels begin to decline around menopause reduced the risk of heart disease, as well as bringing other benefits. In fact, as the 2002 Women's Health Initiative—a prospective, randomized controlled trial—showed, hormone replacement does not protect against heart disease and raises the risk of stroke and breast cancer. The problem was that women using hormone replacement therapy in the observational studies were different in important ways from those who were not (if nothing else, they were being treated by a physician). Those differences, not hormone therapy, accounted for the women's apparently lower risk of cardiovascular disease.

Today's pioneers in the use of health records for CER are well aware that they are conducting observational studies. But they have developed statistical and other methodologies to safeguard against the errors that can bedevil such investigations. The key step is to make sure that it was not something about the

Graphic by Jen Christiansen

patient rather than the treatment that accounted for a given outcome, as was the case in the observational studies of hormone replacement. "There is always the real possibility that people who get one treatment may be different in some ways from people who get another treatment," Selby says. "To adjust for that, you need very detailed data, and Kaiser Permanente has it. It can tell you that patients [in the comparison groups] were identical for all practical purposes or allow you to adjust statistically for any remaining differences."

AND THE BLIND SHALL SEE

OPHTHALMOLOGIST Donald Fong of the Southern California Permanente Medical Group tapped those data to compare two treatments for age-related macular degeneration, the leading cause of severe vision loss in people older than 60 years. Since 2004 physicians had been using Avastin, a cancer drug manufactured by Genentech, against this disease. But that was an off-label use—that is, one for which the company did not have U.S. Food and Drug Administration approval but which physicians are allowed to prescribe anyway. In 2006 the FDA approved Lucentis, also from Genentech, for macular degeneration. Avastin and Lucentis are very similar, but Avastin costs $50 per dose compared with $2,200 for Lucentis. That put physicians in a quandary: Should they continue to use Avastin off-label or switch patients to Lucentis?

Fong knew the question cried out for a scientific comparison. He decided not to conduct a long, expensive randomized controlled clinical trial, however. Instead, from 2005 to 2008, he and his colleagues entered 452 Kaiser patients into a separate registry—all patients who had not been treated before and who received only one drug for macular degeneration. The records showed that 324 people happened to be treated with Avastin and 128 with Lucentis, reflecting individual physician and patient preference rather than the random assignment a clinical trial would use. Although the Avastin patients happened to have worse visual acuity when they began treatment and had an average of two fewer injections over the 12 months they were followed, the improvement in visual acuity was equal with the two drugs, the scientists reported in 2009.

Such an observational study falls short of the statistical purity of a randomized controlled trial. But like other researchers mining health records to do CER, Fong and his colleagues used standard statistical techniques to control for hidden biases in the selection of their population study. They also made sure the Avastin and Lucentis patients were matched in terms of age, severity of vision loss and other key factors. The results, Fong argues, are both scientifically rigorous and more relevant to clinicians than a standard clinical trial. "This study had a much more realistic population," he says. The patients' average age was about 80, and they were not receiving the intense scrutiny and care of those in a clinical trial. "We didn't exclude anyone. That makes it harder for physicians to say, 'This doesn't apply to my patients.' " As it happens, the results from the first year of a randomized controlled trial of Avastin and Lucentis, published online in the *New England Journal of Medicine* in April, support Fong's findings as well.

GETTING THE STATISTICS RIGHT

SCIENTISTS conducting CER by means of electronic medical records are developing a number of techniques to ensure that their results are statistically sound. Most crucial is to make sure that patients in two or more comparison groups—those receiving Lucentis and Avastin, say, or beta blockers and ACE inhibitors—are equivalent. To do this, researchers analyze scores of variables (100 is not unusual), ranging from socioeconomic data to lab results, to see whether any are more commonly found among those patients receiving one treatment and not another. By taking such variables into account, Selby explains, "you wind up comparing people with the same propensity to get a treatment but who actually got either." That eliminates the risk of a hormone replacement therapy–type mistake, where receiving the treatment was actually a marker of better access to care.

In his antihypertension study, for instance, Magid analyzed medical records to identify any patients who were not equally likely to receive both drugs, the ACE inhibitor or beta blocker, such as patients with a preexisting condition that served as a contraindication for one of the two drugs. "We eliminated those cases and were left with only those patients who had an equal probability of being prescribed either an ACE inhibitor or a beta blocker," Magid says. Then he identified patients who had similar health characteristics to reduce the chance that the comparison of the drugs would be biased by, say, one drug having been given to sicker patients.

"We made the populations as equal as possible," he says, based on age, sex, concurrent conditions, vital signs, lab results (for kidney function, for instance), and socioeconomic factors such as education and income. For every 54-year-old white, female high school dropout with a baseline blood pressure of 150 over 80 in the beta blocker group who had these *two* concurrent conditions and took these *three* medications, Magid matched her to another 54-year-old white, female high school dropout with a baseline blood pressure of 150 over 80 in the ACE inhibitor group, who had the same medical conditions and was taking the same drugs. By the time he had finished, Magid had meticulously matched each patient receiving ACE inhibitors to one receiving beta blockers. Patients who could not be matched in this way were dropped from the study.

Because analyzing detailed health records yields results much faster than a prospective, randomized controlled trial, it has saved lives. Kaiser rheumatologist David H. Campen used this methodology when a colleague in academia mentioned that there were hints in lab animal studies that Vioxx, used for pain, might increase the risk of heart attacks and stroke. Analyzing Kaiser's patient records, Campen and his colleagues found exactly that several months before Merck voluntarily withdrew Vioxx from the market in 2004. As it happened, fewer Kaiser pa-

Illustration by Alex Nabaum

tients were taking Vioxx and related drugs, called COX-2 inhibitors, than the national average. COX-2 inhibitors do not pose the same risk of gastrointestinal bleeding as other nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, but not all patients are at risk for such bleeding and so do not need the newer, pricier COX-2 inhibitors. At one point, Campen recalls, COX-2 use was approaching 50 percent of NSAID prescriptions in the U.S., but at Kaiser it stayed below 10 percent.

BANG FOR THE HEALTH CARE BUCK

BEYOND EVALUATING how well different therapies treat a given disease, the new breed of comparative effectiveness researchers aims to compare the costs of those treatments—and to ask whether additional cost buys additional effectiveness. Until now, that question had been off-limits: a core tenet of American medicine has long been that cost considerations have no place in clinical decision making. As a result, CER has, traditionally, not considered cost. Two or more treatments are evaluated and ranked by clinical effectiveness, and that is that. But the soaring costs of health care have increased pressure to choose treatments that deliver the most bang for the health care buck.

Over the past few years, however, cost-effectiveness has been a focus of more and more analysis. In 2006 VA researchers studied patients with a difficult-to-treat form of heart disease that is characterized by diminished blood flow. Some received angioplasty, in which a surgeon widens an obstructed blood vessel (usually with a balloonlike device), and some underwent coronary artery bypass, in which blood flow is rerouted around the blockage with implanted grafts. Each procedure had an impressive three-year survival rate (82 percent with angioplasty and 79 percent with bypass). But total costs for angioplasty were $63,900 compared with $84,400 for bypass. In other words, angioplasty was slightly more effective, as well as less costly. After five years, 75 percent of angioplasty patients were alive, compared with 70 percent of bypass patients, with respective costs of $82,000 and $101,000—again, better survival, lower cost.

The path to using such results to actually control costs is not necessarily straightforward. The 2010 health care reform law bars Medicare from using comparative effectiveness research to decide what to pay for (Avastin but not Lucentis for macular degeneration, say), a concession to legislators who wanted assurance that patients and doctors would remain free to choose any treatment they like and who threatened to vote against the bill without that provision. But Medicare can use the research to set payment rates in a way that would encourage providers to deliver the best care for a given price, a system called "equal payments for equal results." Using the example of macular degeneration, Medicare might pay $50 per injection—which would mean patients who insist on Lucentis, or whose doctor does, would be left with a $2,150 co-payment.

Making people pay more out of pocket is not the goal. It is only the means to the goal, which is to bring patients the most effective treatments—and not to raise the nation's health care bill by subsidizing treatments that cost more for zero additional benefit. "As we move into the era of health care reform, we need to address the issue of how to pay for it," Fong says. "One obvious answer is, you want to pay only for things that work." When two medications work equally well, as he found Avastin and Lucentis did for age-related macular degeneration, the calculus should be easy. But how about when drug A costs 20 times more than drug B but yields only a 5 percent greater benefit, as measured by, for instance, survival, visual acuity, insulin control or number of hospitalizations? "We have to start asking, as a society, whether that marginal improvement is worth the price," he points out. That will surely be a painful conversation, forcing society to grapple with how much we are willing to spend on marginal improvements in health.

THE OBSTACLES TO COME

ALTHOUGH ROOTING OUT ineffective treatments may sound like something patients, physicians and payers would all welcome, in fact, CER has gotten caught in the cross fire of the debates over health care reform. Chief among the charges: that the research will be used to "deny or ration care," as Representative Mike Rogers of Michigan warned in 2009. In fact, the research does not compare whether different kinds of patients benefit from a given treatment as a way to keep one group from receiving the treatment, as "deny or ration" might imply. The goal of comparative effectiveness research is to weed out treatments that are less effective in everyone and substitute a more effective alternative. "There is an assault on CER going on now, saying it's all about health care rationing," says cardiologist Steven Nissen of the Cleveland Clinic. "They're making headway even though that's not what we're talking about. CER is about delivering the best care, not rationing care."

Such qualms are unique to the U.S., health experts say. In no other country do people "view evidence as suspiciously as U.S. stakeholders, including a large proportion of policy makers," argued British researchers in an essay in the journal *Pharmaco-Economics* last year. The U.K. embraced comparative effectiveness research long ago, incorporating its findings into decisions about what its National Health Service will cover. The evidence shows that CER is not a panacea; health care costs are still rising in the U.K.—though not as steeply as in the U.S. But basing health care decisions on CER clearly has not hurt British people, who actually enjoy higher life expectancy than do Americans [*see box on page 53*].

"If there is any country in the world that needs comparative effectiveness research, it's the U.S.," Nissen says. "It's safe to say the U.S. has the least cost-effective medicine in the world. There is so much money wasted that if we eliminated that waste, we could provide health care for everyone." It will be an uphill battle in a country that reveres an individual's right to choose much more than it does science. But comparative effectiveness research is our best hope for improving medical care equitably without breaking the bank. SA

MORE TO EXPLORE

What Is Comparative Effectiveness Research? Answers to frequently asked questions by the Agency for Healthcare Research and Quality. **www.effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1**

The Triple Aim: Care, Health, and Cost. D. M. Berwick et al. in *Health Affairs*, Vol. 27, No. 3, pages 759–769; May 2008. **http://content.healthaffairs.org/content/27/3/759.full**

Money-Driven Medicine. Video documentary produced by Alex Gibney; inspired by Maggie Mahar's book of the same title. **http://moneydrivenmedicine.org**

SCIENTIFIC AMERICAN ONLINE
Health care myths: Find out why more care is not always better, how screening tests can harm and other surprising truths at **ScientificAmerican.com/jul2011/health-care**

CLIMATE CHANGE

THE Last Great Global Warming

Surprising new evidence suggests the pace of the earth's most abrupt prehistoric warm-up paled in comparison to what we face today. The episode has lessons for our future

By Lee R. Kump

Illustration by Ron Miller

Lee R. Kump is a professor of geosciences at Pennsylvania State University and co-author of the book *Dire Predictions: Understanding Global Warming* (DK Adult, 2008). Planetary fevers are his specialty.

POLAR BEARS DRAW MOST VISITORS TO Spitsbergen, the largest island in Norway's Svalbard archipelago. For me, rocks were the allure. My colleagues and I, all geologists and climate scientists, flew to this remote Arctic island in the summer of 2007 to find definitive evidence of what was then considered the most abrupt global warming episode of all time. Getting to the rocky outcrops that might entomb these clues meant a rugged, two-hour hike from our old bunkhouse in the former coal-mining village of Longyearbyen, so we set out early after a night's rest. As we trudged over slippery pockets of snow and stunted plants, I imagined a time when palm trees, ferns and alligators probably inhabited this area.

Back then, around 56 million years ago, I would have been drenched with sweat rather than fighting off a chill. Research had indicated that in the course of a few thousand years—a mere instant in geologic time—global temperatures rose five degrees Celsius, marking a planetary fever known to scientists as the Paleocene-Eocene Thermal Maximum, or PETM. Climate zones shifted toward the poles, on land and at sea, forcing plants and animals to migrate, adapt or die. Some of the deepest realms of the ocean became acidified and oxygen-starved, killing off many of the organisms living there. It took nearly 200,000 years for the earth's natural buffers to bring the fever down.

The PETM bears some striking resemblances to the human-caused climate change unfolding today. Most notably, the culprit behind it was a massive injection of heat-trapping greenhouse gases into the atmosphere and oceans, comparable in volume to what our persistent burning of fossil fuels could deliver in coming centuries. Knowledge of exactly what went on during the PETM could help us foresee what our future will be like. Until recently, though, open questions about the event have made predictions speculative at best. New answers provide sobering clarity. They suggest the consequences of the planet's last great global warming paled in comparison to what lies ahead, and they add new support for predictions that humanity will suffer if our course remains unaltered.

GREENHOUSE CONSPIRACY

TODAY INVESTIGATORS think the PETM unfolded something like this: As is true of our current climate crisis, the PETM began, in a sense, with the burning of fossil fuels. At the time the supercontinent Pangaea was in the final stages of breaking up, and the earth's crust was ripping apart, forming the northeastern Atlantic Ocean. As a result, huge volumes of molten rock and intense heat rose up through the landmass that encompassed Europe and Greenland, baking carbon-rich sediments and perhaps even some coal and oil near the surface. The baking sediments, in turn, released large doses of two strong greenhouse gases, carbon dioxide and methane. Judging by the enormous volume of the eruptions, the volcanoes probably accounted for an initial buildup of greenhouse gases on the order of a few hundred petagrams of carbon, enough to raise global temperature by a couple of degrees. But most analyses, including ours, suggest it took something more to propel the PETM to its hottest point.

A second, more intense warming phase began when the volcano-induced heat set other types of gas release into motion. Natural stirring of the oceans ferried warmth to the cold seabed, where it apparently destabilized vast stores of frozen methane hydrate deposits buried within. As the hydrates thawed, methane gas bubbled up to the surface, adding more carbon into the atmosphere. Methane in the atmosphere traps heat much more effectively than CO_2 does, but it converts quickly to CO_2. Still, as long as the methane release continued, elevated concentrations

IN BRIEF

Global temperature rose five degrees Celsius 56 million years ago in response to a massive injection of greenhouse gases into the atmosphere.

That intense gas release was only 10 percent of the rate at which heat-trapping greenhouse gases are building up in the atmosphere today.

The speed of today's rise is more troubling than the absolute magnitude, because adjusting to rapid climate change is very difficult.

of that gas would have persisted, strongly amplifying the greenhouse effect and the resulting temperature rise.

A cascade of other positive feedbacks probably ensued at the same time as the peak of the hydrate-induced warming, releasing yet more carbon from reservoirs on land. The drying, baking or burning of any material that is (or once was) living emits greenhouse gases. Droughts that would have resulted in many parts of the planet, including the western U.S. and western Europe, most likely exposed forests and peat lands to desiccation and, in some cases, widespread wildfires, releasing even more CO_2 to the atmosphere. Fires smoldering in peat and coal seams, which have been known to last for centuries in modern times, could have kept the discharge going strong.

Thawing permafrost in polar regions probably exacerbated the situation as well. Permanently frozen ground that locks away dead plants for millions of years, permafrost is like frozen hamburger in the freezer. Put that meat on the kitchen counter, and it rots. Likewise, when permafrost defrosts, microbes consume the thawing remains, burping up lots of methane. Scientists worry that methane belches from the thawing Arctic could greatly augment today's fossil-fuel-induced warming. The potential contribution of thawing permafrost during the PETM was even more dramatic. The planet was warmer then, so even before the PETM, Antarctica lacked the ice sheets that cover the frozen land today. But that continent would still have had permafrost—all essentially "left on the counter" to thaw.

When the gas releases began, the oceans absorbed much of the CO_2 (and the methane later converted to CO_2). This natural carbon sequestration helped to offset warming at first. Eventually, though, so much of the gas seeped into the deep ocean that it created a surplus of carbonic acid, a process known as acidification. Moreover, as the deep sea warmed, its oxygen content dwindled (warmer water cannot hold as much of this life-sustaining gas as cold water can). These changes spelled disaster for certain microscopic organisms called foraminifera, which lived on the seafloor and within its sediments. The fossil record reveals their inability to cope: 30 to 50 percent of those species went extinct.

CORE KNOWLEDGE

THAT A SPECTACULAR RELEASE of greenhouse gases fueled the PETM has been clear since 1990, when a pair of California-based researchers first identified the event in a multimillion-year climate record from a sediment core drilled out of the seabed near Antarctica. Less apparent were the details, including exactly how much gas was released, which gas predominated, how long the spewing lasted and what prompted it.

In the years following that discovery, myriad scientists analyzed hundreds of other deep-sea sediment cores to look for answers. As sediments are laid down slowly, layer by layer, they trap minerals—including the skeletal remains of sea life—that retain signatures of the composition of the surrounding oceans or atmosphere as well as life-forms present at the time of deposition. The mix of different forms, or isotopes, of oxygen atoms in the skeletal remains revealed the temperature of the water, for instance.

When well preserved, such cores offer a beautiful record of climate history. But many of those that included the PETM were not in good shape. Parts were missing, and those left behind had been degraded by the passage of time. Seafloor sediment is typically rich in the mineral calcium carbonate, the same chemical compound in antacid tablets. During the PETM, ocean acidification dissolved away much of the carbonate in the sediments in exactly the layers where the most extreme conditions of the PETM era should have been represented.

It is for this reason that my colleagues and I met up in Spitsbergen in 2007 with a group of researchers from England, Norway and the Netherlands, under the auspices of the Worldwide Universities Network. We had reason to believe that rocks from this part of the Arctic, composed almost entirely of mud and clay, could provide a more complete record—and finally resolve some of the unanswered questions about that ancient warming event. Actually we intended to pluck our samples from an eroded plateau, not from underneath the sea. The sediments we sought were settled into an ancient ocean basin, and tectonic forces at play since the PETM had thrust that region up above sea level, where ice age glaciers later sculpted it into Spitsbergen's spectacular range of steep mountains and wide valleys.

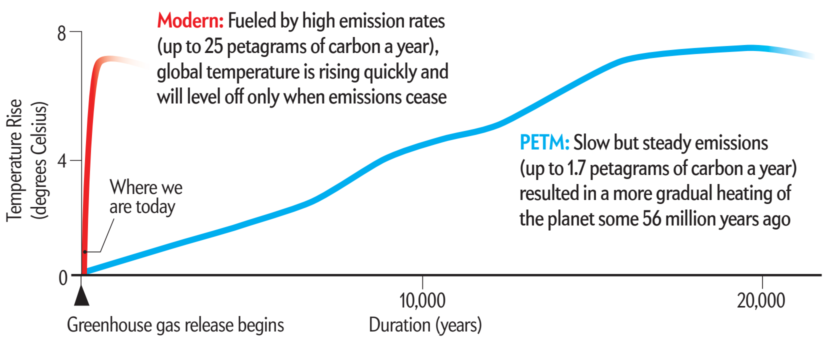
After that first scouting trip from Longyearbyen, while devising plans for fieldwork and rock sampling, we made a discovery that saved much heavy lifting. We learned from a forward-thinking local geologist that a Norwegian mining company he worked for had cored through sediment layers covering the PETM era years earlier. He had taken it on himself to preserve kilometers

SURPRISING FINDING

Now and Then

How fast the world warms depends on how fast greenhouse gases build in the atmosphere. Projections anticipate a warm-up of about eight degrees Celsius by 2400 if fossil-fuel burning and carbon sequestration go unaltered. The projected carbon release, about 5,000 petagrams, is similar in volume to what fueled the Paleocene-Eocene Thermal Maximum, or PETM, but the past rate, once thought to be rapid, was slower than today's.

Global temperature is rising much more quickly today than it did during the PETM



SOURCES: "THE MILLENNIAL ATMOSPHERIC LIFETIME OF ANTHROPOGENIC CO_2," BY DAVID ARCHER AND VICTOR BROVKIN, IN *CLIMATIC CHANGE*, VOL. 90; 2008 (*modern curve*); "MODERN RATES OF FOSSIL FUEL BURNING EXCEED RATES OF FOSSIL CARBON EMISSION DURING THE PALEOCENE-EOCENE THERMAL MAXIMUM," BY YING CUI ET AL., IN *NATURE GEOSCIENCE* (IN PRESS) (*PETM curve*)

Graphic by Jen Christiansen

of that core on the off chance that scientists would one day find them useful. He led us to a large metal shed on the outskirts of town where the core is now housed, since cut into 1.5-meter-long cylinders stored in hundreds of flat wood boxes. Our efforts for the rest of that trip, and during a second visit in 2008, were directed at obtaining samples from selected parts of that long core.

Back in the lab, over several years, we extracted from those samples the specific chemical signatures that could tell us about the state of the earth as it passed into and out of the PETM. To understand more about the greenhouse gas content of the air, we studied the changing mix of carbon isotopes, which we gleaned mostly from traces of organic matter preserved in the clay. By making extractions and analyses for more than 200 layers of the core, we could piece together how these factors changed over time. As we suspected, the isotope signature of carbon shifted dramatically in the layers we knew to be about 56 million years old.

STRETCHING TIME

OUR ARCTIC CORES turned out to be quite special. The first to record the full duration of the PETM warm-up and recovery, they provided a much more complete snapshot of the period when greenhouse gases were being released to the atmosphere. We suspected that the unprecedented fidelity of these climate records would ultimately provide the most definitive answers to date about the amount, source and duration of gas release. But to get those results, we had to go beyond extrapolations from the composition and concentration of materials in the cores. We asked Ying Cui, my graduate student at Pennsylvania State University, to run a sophisticated computer model that simulated the warming based on what we knew about the changes in the carbon isotope signatures from the Arctic cores and the degree of dissolution of seafloor carbonate from deep-sea cores.

Cui tried different scenarios, each one taking a month of computer time to play out the full PETM story. Some assumed greater contributions from methane hydrates, for instance; others assumed more from CO_2 sources. The scenario that best fit the physical evidence required the addition of between 3,000 and 10,000 petagrams of carbon into the atmosphere and ocean, more than the volcanoes or methane hydrates could provide; permafrost or peat and coal must have been involved. This estimate falls on the high side of those made previously based on isotope signatures from other cores and computer models. But what surprised us most was that this gas release was spread out over approximately 20,000 years—a time span between twice and 20 times as long as anyone has projected previously. That lengthy duration implies that the rate of injection during the PETM was less than two petagrams a year—a mere fraction of the rate at which the burning of fossil fuels is delivering greenhouse gases into the air today. Indeed, CO_2 concentrations are rising probably 10 times faster now than they did during the PETM.

This new realization has profound implications for the future. The fossil record tells us that the speed of climate change has more impact on how life-forms and ecosystems fare than does the extent of the change. Just as you would prefer a hug from a friend to a punch in the stomach, life responds more favorably to slow changes than to abrupt ones. Such was the case during an extreme shift to a hothouse climate during the Cretaceous period (which ended 65 million years ago, when an asteroid impact killed the dinosaurs). The total magnitude of greenhouse warming during the Cretaceous was similar to that of the PETM, but that former episode unfolded over millions, rather than thousands, of years. No notable extinctions occurred; the planet and its inhabitants had plenty of time to adjust.

For years scientists considered the PETM to be the supreme example of the opposite extreme: the fastest climate shift ever known, rivaling the gloomiest projections for the future. In that light, the PETM's outcomes did not seem so bad. Aside from the unlucky foraminifera in the deep sea, all animals and plants apparently survived the heat wave—even if they had to make some serious adaptations to do so. Some organisms shrank. In particular, mammals of the PETM are smaller than both their predecessors and descendants. They evolved this way presumably because smaller bodies are better at dissipating heat than larger ones. Burrowing insects and worms, too, dwarfed.

A great poleward migration saved other creatures. Some even thrived in their expanded territories. At sea, the dinoflagellate *Apectodinium,* usually a denizen of the subtropics, spread to the Arctic Ocean. On land, many animals that had been confined to the tropics made their way into North America and Europe for the first time, including turtles and hoofed mammals. In the case of mammals, this expansion opened up myriad opportunities to evolve and fill new niches, with profound implications for human beings: this grand diversification included the origin of primates.

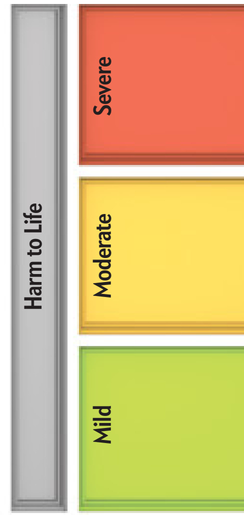
TOO FAST?

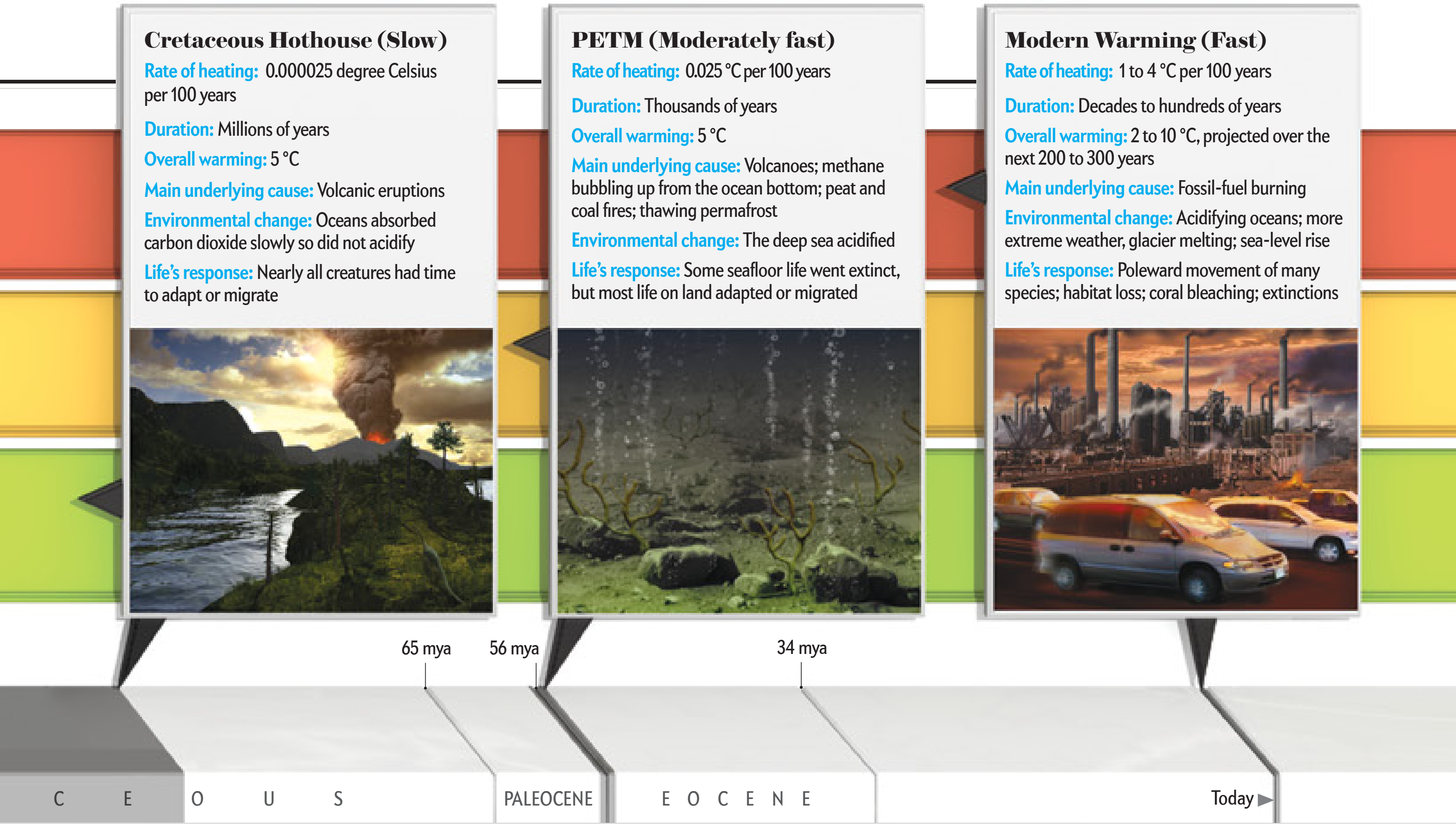
NOW THAT WE KNOW the pace of the PETM was moderate at worst and not really so fast, those who have invoked its rather innocuous biological consequences to justify impenitence about fossil-fuel combustion need to think again. By comparison, the

IMPLICATIONS

Lessons from Past Warmings

Planetary fevers that come on suddenly—such as the scenario unfolding today—are much harder on life than the slower ones are. The fossil record shows that the slow shift to a hothouse from 120 million to 90 million years ago, during the Cretaceous period, was innocuous relative to the PETM, which was 1,000 times more abrupt. The latter episode has long been analyzed for clues to how our own warming trend will play out, but today's much faster temperature change suggests that the consequences for life on earth will be harsher than anything that has come before.





climate shift currently under way is happening at breakneck speed. In a matter of decades, deforestation and the cars and coal-fired power plants of the industrial revolution have increased CO_2 by more than 30 percent, and we are now pumping nine petagrams of carbon into the atmosphere every year. Projections that account for population growth and increased industrialization of developing nations indicate that rate may reach 25 petagrams a year before all fossil-fuel reserves are exhausted.

Scientists and policy makers grappling with the potential effects of climate change usually focus on end products: How much ice will melt? How high will sea level rise? The new lesson from PETM research is that they should also ask: How fast will these changes occur? And will the earth's inhabitants have time to adjust? If change occurs too fast or if barriers to migration or adaptation loom large, life loses: animals and plants go extinct, and the complexion of the world is changed for millennia.

Because we are in the early interval of the current planetary fever, it is difficult to predict what lies ahead. But already we know a few things. As summarized in recent reports from the Intergovernmental Panel on Climate Change, ecosystems have been responding sensitively to the warming. There is clear evidence of surface-water acidification and resulting stress on sea life [see "Threatening Ocean Life from the Inside Out," by Marah J. Hardt and Carl Safina; Scientific American, August 2010]. Species extinctions are on the rise, and shifting climate zones have already put surviving plants and animals on the move, often with the disease-bearing pests and other invasive species winning out in their new territories. Unlike those of the PETM, modern plants and animals now have roads, railways, dams, cities and towns blocking their migratory paths to more suitable climate. These days most large animals are already penned into tiny areas by surrounding habitat loss; their chances of moving to new latitudes to survive will in many cases be nil.

Furthermore, glaciers and ice sheets are melting and driving sea-level rise; coral reefs are increasingly subject to disease and heat stress; and episodes of drought and flooding are becoming more common. Indeed, shifts in rainfall patterns and rising shorelines as polar ice melts may contribute to mass human migrations on a scale never before seen. Some have already begun [see "Casualties of Climate Change," by Alex de Sherbinin, Koko Warner and Charles Ehrhart; Scientific American, January].

Current global warming is on a path to vastly exceed the PETM, but it may not be too late to avoid the calamity that awaits us. To do so requires immediate action by all the nations of the world to reduce the buildup of atmospheric carbon dioxide—and to ensure that the Paleocene-Eocene Thermal Maximum remains the last great global warming. SA

MORE TO EXPLORE

The Paleocene-Eocene Thermal Maximum: A Perturbation of Carbon Cycle, Climate, and Biosphere with Implications for the Future. Francesca A. McInerney and Scott L. Wing in *Annual Review of Earth and Planetary Sciences,* Vol. 39, pages 489–516; May 2011.

America's Climate Choices. Committee on America's Climate Choices, National Research Council of the National Academies. The National Academies Press, 2011.

Slow Release of Fossil Carbon during the Palaeocene-Eocene Thermal Maximum. Ying Cui et al. in *Nature Geoscience* (in press).

SCIENTIFIC AMERICAN ONLINE
See a slide show of the author and his collaborators in the field at ScientificAmerican.com/jul2011/climate-change

Illustrations by Ron Miller, Graphic by Emily Cooper

UNDERGROUND RAILROAD

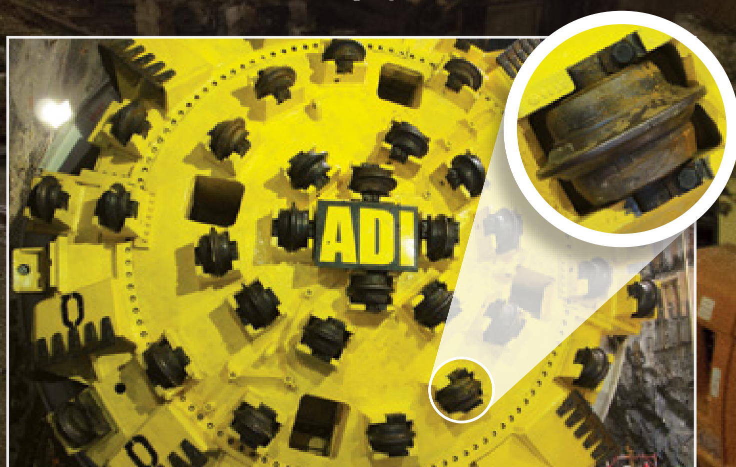
A peek inside New York City's subway line of the future

By Anna Kuchment, staff editor

SIXTY-FIVE FEET BELOW THE STREETS OF MANHATTAN, WORKERS are digging the city's first new subway line since the 1940s. The Second Avenue subway, to be named the T line, will eventually stretch from 125th Street in East Harlem to Hanover Square in the financial district. The first stretch of the line, from 96th Street to 63rd Street, is set to open in December 2016, carrying more than 200,000 passengers every day.

SCIENTIFIC AMERICAN visited the base of operations for the dig this past April, as engineers completed the downtown tunnel (*right*) and set to work on the uptown side (*left*). A 700-foot-long tunnel-boring machine, or TBM, does the actual digging, moving at a rate of up to 100 feet a day through the city's bedrock, a blend of granite, mica, gneiss and garnet known as Manhattan schist (*inset*). "The rock in the tunnel is twice as strong as concrete, and still the TBM cuts through it like a piece of cake," says project manager Alaeden Jlelaty of Swedish construction firm Skanska. The TBM, nicknamed "Adi" for the granddaughter of an MTA official, delivers 2.99 million pounds of thrust, the equivalent of 12 Boeing 747s.

Little of the rock the machine shatters goes to waste. Each day trucks deliver debris from the tunnel to construction sites around the city, where it is used for landscaping and land reclamation. SA



Cut! The TBM features a 22-foot-tall, 200-ton cutter head with 44 rotating steel disks that workers change every two to three weeks.

BENJAMIN KABAK

SCIENTIFIC AMERICAN ONLINE
More images and readings at ScientificAmerican.com/jul2011/subway

Photograph by Floto + Warner

Trevor D. Lamb is an investigator in the department of neuroscience at the John Curtin School of Medical Research and in the ARC Centre of Excellence in Vision Science at the Australian National University in Canberra. His research focuses on the rod and cone photoreceptors of the vertebrate retina.

BIOLOGY

EVOLUTION OF THE EYE

Scientists now have a clear vision of how our notoriously complex eye came to be

By Trevor D. Lamb

THE HUMAN EYE IS AN EXQUISITELY COMPLICATED ORGAN. IT ACTS LIKE A CAMERA TO collect and focus light and convert it into an electrical signal that the brain translates into images. But instead of photographic film, it has a highly specialized retina that detects light and processes the signals using dozens of different kinds of neurons. So intricate is the eye that its origin has long been a cause célèbre among creationists and intelligent design proponents, who hold it up as a prime example of what they term irreducible complexity—a system that cannot function in the absence of any of its components and that therefore cannot have evolved naturally from a more primitive form. Indeed, Charles Darwin himself acknowledged in *On the Origin of Species*—the 1859 book detailing his theory of evolution by natural selection—that it might seem absurd to think the eye formed by natural selection. He nonetheless firmly believed that the eye did evolve in that way, despite a lack of evidence for intermediate forms at the time.

Direct evidence has continued to be hard to come by. Whereas scholars who study the evolution of the skeleton can readily document its metamorphosis in the fossil record, soft-tissue structures rarely fossilize. And even when they do, the fossils do not preserve nearly enough detail to establish how the structures evolved. Still, biologists have recently made significant advances in tracing the origin of the eye—by studying how it forms in developing embryos and by comparing eye structure and genes across species to reconstruct when key traits arose. The results indicate that our kind of eye—the type common across vertebrates—took shape in less than 100 million years, evolving from a simple light sensor for circadian (daily) and seasonal rhythms around 600 million years ago to an optically and neurologically sophisticated organ by 500 million years ago. More than 150 years after Darwin published his

SPECIMEN COURTESY OF THE EYE-BANK FOR SIGHT RESTORATION, NEW YORK (WWW.EYEDONATION.ORG)

Photograph by Dan Saelinger

groundbreaking theory, these findings put the nail in the coffin of irreducible complexity and beautifully support Darwin's idea. They also explain why the eye, far from being a perfectly engineered piece of machinery, exhibits a number of major flaws—these flaws are the scars of evolution. Natural selection does not, as some might think, result in perfection. It tinkers with the material available to it, sometimes to odd effect.

To understand how our eye originated, one needs to know something about events that occurred in deep time. We humans have an unbroken line of ancestors stretching back nearly four billion years to the beginning of life on earth. Around a billion years ago simple multicellular animals diverged into two groups: one had a radially symmetrical body plan (a top side and bottom side but no front or back), and the other—which gave rise to most of the organisms we think of as animals—was bilaterally symmetrical, with left and right sides that are mirror images of one another and a head end. The bilateria themselves then diverged around 600 million years ago into two important groups: one that gave rise to the vast majority of today's spineless creatures, or invertebrates, and one whose descendants include our own vertebrate lineage. Soon after these two lineages parted ways, an amazing diversity of animal body plans proliferated—the so-called Cambrian explosion that famously left its mark in the fossil record of around 540 million to 490 million years ago. This burst of evolution laid the groundwork for the emergence of our complex eye.

COMPOUND VS. CAMERA

THE FOSSIL RECORD shows that during the Cambrian explosion two fundamentally different styles of eye arose. The first seems to have been a compound eye of the kind seen today in all adult insects, spiders and crustaceans—part of an invertebrate group collectively known as the arthropods. In this type of eye, an array of identical imaging units, each of which constitutes a lens or reflector, beams light to a handful of light-sensitive elements called photoreceptors. Compound eyes are very effective for small animals in offering a wide-angle view and moderate spatial resolution in a small volume. In the Cambrian, such visual ability may have given trilobites and other ancient arthropods a survival advantage over their visually impaired contemporaries. Compound eyes are impractical for large animals, however, because the eye size required for high-resolution vision would be overly large. Hence, as body size increased, so, too, did the selective pressures favoring the evolution of another type of eye: the camera variety.

In camera-style eyes, the photoreceptors all share a single light-focusing lens, and they are arranged as a sheet (the retina) that lines the inner surface of the wall of the eye. Squid and octopuses have a camera-style eye that superficially resembles our own, but their photoreceptors are the same kind found in insect eyes. Vertebrates possess a different style of photoreceptor, which in jawed vertebrates (including ourselves) comes in two varieties: cones for daylight vision and rods for nighttime vision.

Several years ago Edward N. Pugh, Jr., then at the University of Pennsylvania, and Shaun P. Collin, then at the University of Queensland in Australia, and I teamed up to try to figure out how these different types of photoreceptors could have evolved. What we found went beyond answering that question to provide a compelling scenario for the origin of the vertebrate eye.

DEEP ROOTS

LIKE OTHER BIOLOGISTS before us, Pugh, Collin and I observed that many of the hallmark features of the vertebrate eye are the same across all living representatives of a major branch of the vertebrate tree: that of the jawed vertebrates. This pattern suggests that jawed vertebrates inherited the traits from a common ancestor and that our eye had already evolved by around 420 million years ago, when the first jawed vertebrates (which probably resembled modern-day cartilaginous fish such as sharks) patrolled the seas. We reasoned that our camera-style eye and its photoreceptors must therefore have still deeper roots, so we turned our attention to the more primitive jawless vertebrates, with which we share a common ancestor from roughly 500 million years ago.

We wanted to examine the anatomy of such an animal in detail and thus decided to focus on one of the few modern-day animals in this group: the lamprey, an eel-like fish with a funnel-shaped mouth built for sucking rather than biting. It turns out that this fish, too, has a camera-style eye complete with a lens, an iris and eye muscles. The lamprey's retina even has a three-layered structure like ours, and its photoreceptor cells closely resemble our cones, although it has apparently not evolved the more sensitive rods. Furthermore, the genes that govern many aspects of light detection, neural processing and eye development are the same ones that direct these processes in jawed vertebrates.

These striking similarities to the eye of jawed vertebrates are far too numerous to have arisen independently. Instead an eye essentially identical to our own must have been present in the common ancestor of the jawless and jawed vertebrates 500 million years ago. At this point, my colleagues and I could not help but wonder whether we could trace the origin of the eye and its photoreceptors back even further. Unfortunately, there are no living representatives of lineages that split off from our line in the preceding 50 million years, the next logical slice of time to study. But we found clues in the eye of an enigmatic beast called the hagfish.

Like their close relatives the lampreys, hagfish are eel-shaped, jawless fish. They typically live on the ocean floor, where they feed on crustaceans and fallen carcasses of other marine creatures. When threatened, they exude an extremely viscous slime, hence the nickname "slime eels." Although hagfish are vertebrates, their eye departs profoundly from the vertebrate norm. The hagfish eye lacks a cornea, iris, lens and all of the usual supporting muscles. Its retina contains just two layers of cells rather than three. Furthermore, each eye is buried deep underneath a translucent patch of skin. Observations of hagfish behavior sug-

IN BRIEF

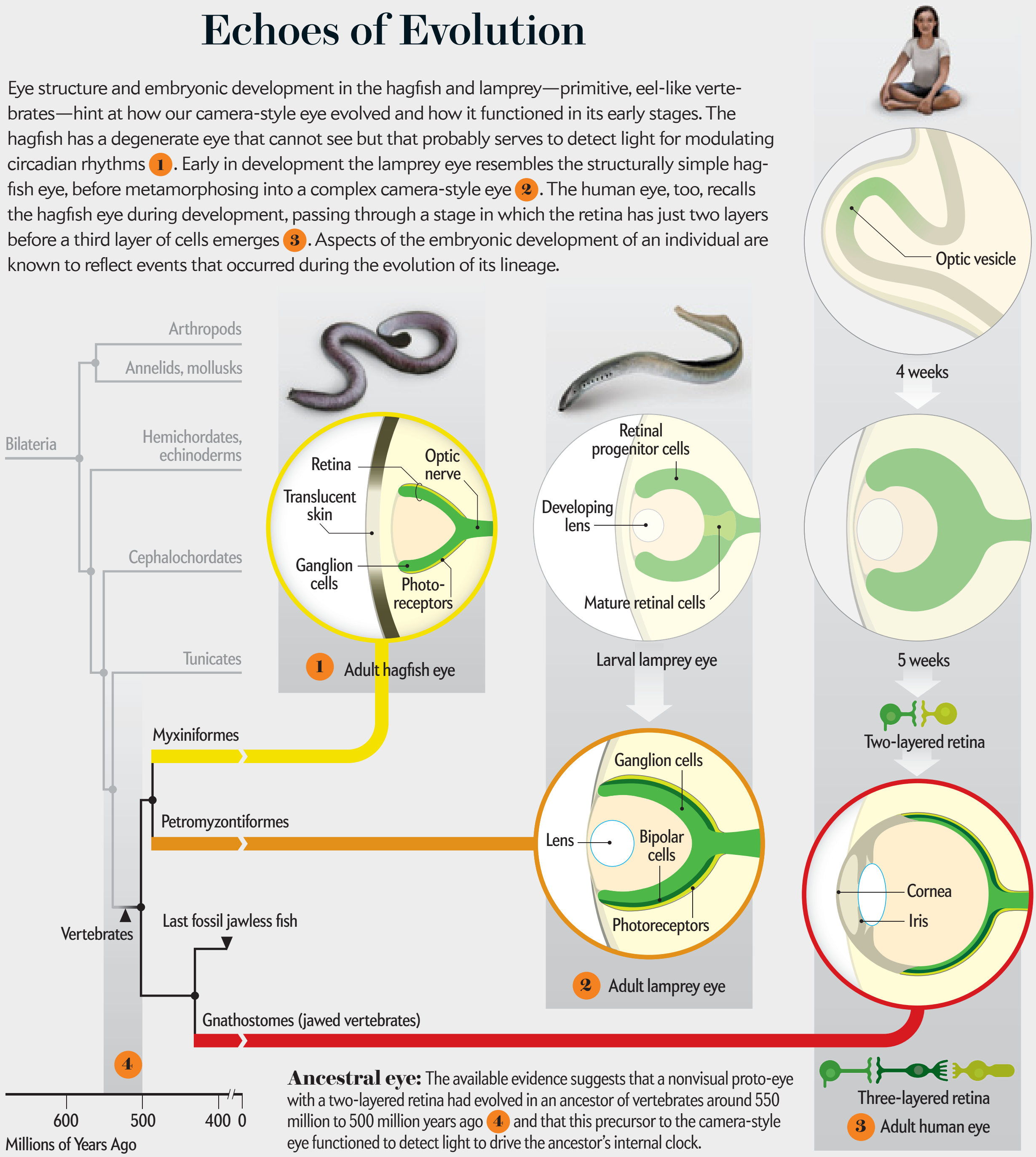
The eyes of vertebrate animals are so complex that creationists have long argued that they could not have formed by natural selection.

Soft tissues rarely fossilize. But by comparing eye structures and embryological development of the eye in vertebrate species, scientists have gained crucial insights into the organ's origin.

These findings suggest that our camera-style eye has surprisingly ancient roots and that prior to acquiring the elements necessary to operate as a visual organ it functioned to detect light for modulating our long-ago ancestors' circadian rhythms.

Echoes of Evolution

Eye structure and embryonic development in the hagfish and lamprey—primitive, eel-like vertebrates—hint at how our camera-style eye evolved and how it functioned in its early stages. The hagfish has a degenerate eye that cannot see but that probably serves to detect light for modulating circadian rhythms (1). Early in development the lamprey eye resembles the structurally simple hagfish eye, before metamorphosing into a complex camera-style eye (2). The human eye, too, recalls the hagfish eye during development, passing through a stage in which the retina has just two layers before a third layer of cells emerges (3). Aspects of the embryonic development of an individual are known to reflect events that occurred during the evolution of its lineage.



Ancestral eye: The available evidence suggests that a nonvisual proto-eye with a two-layered retina had evolved in an ancestor of vertebrates around 550 million to 500 million years ago (4) and that this precursor to the camera-style eye functioned to detect light to drive the ancestor's internal clock.

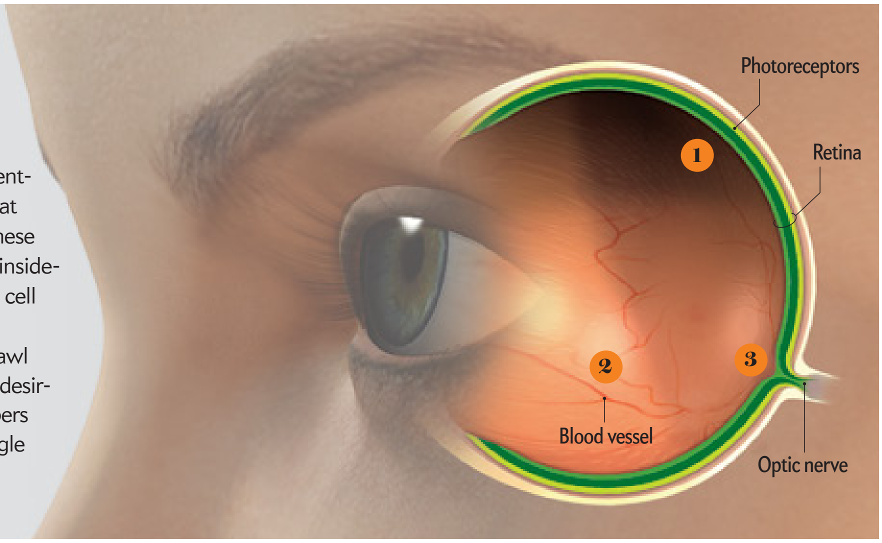
gest that the animals are virtually blind, locating carrion with their keen sense of smell.

The hagfish shares a common ancestor with the lamprey, and this ancestor presumably had a camera-style eye like the lamprey's. The hagfish eye must therefore have degenerated from that more advanced form. That it still exists in this diminished state is telling. We know from blind cavefish, for instance, that the eye can undergo massive degeneration and can even be lost altogether in as little as 10,000 years. Yet the hagfish eye, such as it is, has hung on for hundreds of millions of years. This persistence suggests that even though the animal cannot use its eye to see in the dim ocean depths, the organ is somehow important for survival. The discovery also has other implications. The hagfish eye may have ended up in its rudimentary state by way of a failure of development, so its current structure may be representative of the architecture of an earlier evolutionary stage. The operation of the hagfish eye could thus throw light on how the proto-eye functioned before evolving into a visual organ.

Hints about the role the hagfish eye might play came from taking a closer look at the animal's retina. In the standard three-

Scars of Evolution

The vertebrate eye, far from being intelligently designed, contains numerous defects that attest to its evolutionary origin. Some of these flaws degrade image quality, including an inside-out retina that forces light to pass through cell bodies and nerve fibers before hitting the photoreceptors (1); blood vessels that sprawl across the retina's inner surface, casting undesirable shadows onto the retina (2); nerve fibers that gather together to push through a single opening in the retina to become the optic nerve, creating a blind spot (3).



layered vertebrate retina, the cells in the middle layer, known as bipolar cells, process information from the photoreceptors and communicate the results to the output neurons, whose signals travel to the brain for interpretation. The two-layered hagfish retina, however, lacks the intervening bipolar cells, which means that the photoreceptors connect directly to the output neurons. In this regard, the wiring of the hagfish retina closely resembles that of the so-called pineal gland, a small, hormone-secreting body in the vertebrate brain. The pineal gland modulates circadian rhythms, and in nonmammalian vertebrates it contains photoreceptor cells that connect directly to output neurons with no intermediary cells; in mammals those cells have lost their ability to detect light.

Based in part on this parallel to the pineal gland, my collaborators and I proposed in 2007 that the hagfish eye is not involved in vision but instead provides input to the part of the animal's brain that regulates crucial circadian rhythms, as well as seasonal activities such as feeding and breeding. Perhaps, then, the ancestral eye of proto-vertebrates living between 550 million and 500 million years ago first served as a nonvisual organ and only later evolved the neural processing power and optical and motor components needed for spatial vision.

Studies of the embryological development of the vertebrate eye support this notion. When a lamprey is in the larval stage, it lives in a streambed and, like the hagfish, is blind. At that point in its young life, its eye resembles the hagfish eye in being structurally simple and buried below the skin. When the larva undergoes metamorphosis, its rudimentary eye grows substantially and develops a three-layered retina; a lens, cornea and supporting muscles all form. The organ then erupts at the surface as a camera-style vertebrate eye. Because many aspects of the development of an individual mirror events that occurred during the evolution of its ancestors, we can, with caution, use the developing lamprey eye to inform our reconstruction of how the eye evolved.

During embryological development the mammalian eye, too, exhibits telltale clues to its evolutionary origin. Benjamin E. Reese and his collaborators at the University of California, Santa Barbara, have found that the circuitry of the mammalian retina starts out rather like that of the hagfish, with the photoreceptors connecting directly to the output neurons. Then, over a period of several weeks, the bipolar cells mature and insert themselves between the photoreceptors and the output neurons. This sequence is exactly the developmental pattern one would expect to see if the vertebrate retina evolved from a two-layered circadian organ by adding processing power and imaging components. It therefore seems entirely plausible that this early, simple stage of development represents a holdover from a period in evolution before the invention of bipolar cell circuitry in the retina and before the invention of the lens, cornea and supporting muscles.

RISE OF THE RECEPTORS

WHILE WE WERE STUDYING the development of the three layers of the retina, another question related to the eye's evolution occurred to us. Photoreceptor cells across the animal kingdom fall into two distinct classes: rhabdomeric and ciliary. Until recently, many scientists thought that invertebrates used the rhabdomeric class, whereas vertebrates used the ciliary class, but in fact, the situation is more complicated. In the vast majority of organisms, ciliary photoreceptors are responsible for sensing light for nonvisual purposes—to regulate circadian rhythms, for example. Rhabdomeric receptors, in contrast, sense light for the express purpose of enabling vision. Both the compound eyes of arthropods and the camera-style eyes of mollusks such as the octopus, which evolved independently of the camera-style eyes of vertebrates, employ rhabdomeric photoreceptors. The vertebrate eye, however, uses the ciliary class of photoreceptors to sense light for vision.

In 2003 Detlev Arendt of the European Molecular Biology Laboratory in Heidelberg, Germany, reported evidence that our eye still retains the descendants of rhabdomeric photoreceptors, which have been greatly modified to form the output neurons that send information from the retina to the brain. This discovery means that our retina contains the descendants of both classes of photoreceptors: the ciliary class, which has always comprised photoreceptors, and the rhabdomeric class, transformed into output neurons. Pressing an existing structure into use for a new purpose is exactly how evolution works, and so the discovery that the ciliary and rhabdomeric photoreceptors play different roles in our eye than in the eye of invertebrates adds still more weight to the evidence that the vertebrate eye was constructed by natural pro-

Illustration by Don Foley

cesses. We wondered, though, what kinds of environmental pressures might have pushed those cells to take on those new roles.

To try to understand why the ciliary photoreceptors triumphed as the light sensors of the vertebrate retina, whereas the rhabdomeric class evolved into projection neurons, I analyzed the properties of their respective light-sensing pigments, or rhodopsins, so named for the opsin protein molecule they contain. In 2004 Yoshinori Shichida of Kyoto University in Japan and his colleagues had shown that early in the evolution of vertebrate visual pigments, a change had occurred that made the light-activated form of the pigment more stable and hence more active. I proposed that this change also blocked the route for reconversion of the activated rhodopsin back to its inactive form, which for rhabdomeric rhodopsins uses the absorption of a second photon of light; thus, of necessity, a biochemical pathway was needed to reset the molecule in readiness to signal light again. Once these two elements were in place, I hypothesized, the ciliary photoreceptors would have had a distinct advantage over rhabdomeric photoreceptors in environments such as the deep ocean, where light levels are very low. As a result, some early chordates (ancestors of the vertebrates) may have been able to colonize ecological niches inaccessible to animals that relied on rhabdomeric photoreceptors—not because the improved ciliary opsin conferred better vision (the other essential components of the camera-style eye had yet to evolve) but because it provided an improved way of sensing the light that enables circadian and seasonal clocks to keep time.

For these ancient chordates dwelling in darker realms, the less sensitive rhabdomeric photoreceptors they had in addition to the ciliary ones would have been virtually useless and so would have been free to take on a new role: as neurons that transmit signals to the brain. (At that point, they no longer needed opsin, and natural selection would have eliminated it from these cells.)

AN EYE IS BORN

NOW THAT MY COLLEAGUES and I had an idea of how the components of the vertebrate retina originated, we wanted to figure out how the eye evolved from a light-sensing but nonvisual organ into an image-forming one by around 500 million years ago. Here again we found clues in developing embryos. Early in development, the neural structure that gives rise to the eye bulges out on either side to form two sacs, or vesicles. Each of these vesicles then folds in on itself to form a C-shaped retina that lines the interior of the eye. Evolution probably proceeded in much the same way. We postulate that a proto-eye of this kind—with a C-shaped, two-layered retina composed of ciliary photoreceptors on the exterior and output neurons derived from rhabdomeric photoreceptors on the interior—had evolved in an ancestor of vertebrates between 550 million and 500 million years ago, serving to drive its internal clock and perhaps help it to detect shadows and orient its body properly.

In the next stage of embryological development, as the retina is folding inward against itself, the lens forms, originating as a thickening of the embryo's outer surface, or ectoderm, that bulges into the curved empty space formed by the C-shaped retina. This protrusion eventually separates from the rest of the ectoderm to become a free-floating element. It seems likely that a broadly similar sequence of changes occurred during evolution. We do not know exactly when this modification happened, but in 1994 researchers at Lund University in Sweden showed that the optical components of the eye could have easily evolved within a million years. If so, the image-forming eye may have arisen from the nonvisual proto-eye in a geologic instant.

With the advent of the lens to capture light and focus images, the eye's information-gathering capability increased dramatically. This augmentation would have created selective pressures favoring the emergence of improved signal processing in the retina beyond what the simple connection of photoreceptors to output neurons afforded. Evolution met this need by modifying the cell maturation process so that some developing cells, instead of forming ciliary photoreceptors, instead become retinal bipolar cells that insert themselves between the photoreceptor layer and the output neuron layer. This is why the retina's bipolar cells so closely resemble rod and cone cells, although they lack rhodopsin and receive input not from light but instead from the chemical (called a neurotransmitter) released by the photoreceptors.

Although camera-style eyes provide a wide field of view (typically of around 180 degrees), in practice our brain can sample only a fraction of the available information at any given time because of the limited number of nerve fibers linking our eye to our brain. The earliest camera-style eyes no doubt faced an even more severe limitation, because they presumably had even fewer nerve fibers. Thus, there would have been considerable selective pressure for the evolution of muscles to move the eye. Such muscles must have been present by 500 million years ago because the arrangement of these muscles in the lamprey, whose lineage dates back that far, is almost identical to that of jawed vertebrates, including humans.

For all the ingenious features evolution built into the vertebrate eye, there are a number of decidedly inelegant traits. For instance, the retina is inside out, so light has to pass through the whole thickness of the retina—through the intervening nerve fibers and cell bodies that scatter the light and degrade image quality—before reaching the light-sensitive photoreceptors. Blood vessels also line the inner surface of the retina, casting unwanted shadows onto the photoreceptor layer. The retina has a blind spot where the nerve fibers that run across its surface congregate before tunneling out through the retina to emerge behind it as the optic nerve. The list goes on and on.

These defects are by no means inevitable features of a camera-style eye because octopuses and squid independently evolved camera-style eyes that do not suffer these deficiencies. Indeed, if engineers were to build an eye with the flaws of our own, they would probably be fired. Considering the vertebrate eye in an evolutionary framework reveals these seemingly absurd shortcomings as consequences of an ancient sequence of steps, each of which provided benefit to our long-ago vertebrate ancestors even before they could see. The design of our eye is not intelligent—but it makes perfect sense when viewed in the bright light of evolution. SA

MORE TO EXPLORE

Evolution of the Vertebrate Eye: Opsins, Photoreceptors, Retina and Eye Cup. Trevor D. Lamb et al. in *Nature Reviews Neuroscience,* Vol. 8, pages 960–975; December 2007.

The Evolution of Eyes. Special issue of *Evolution: Education and Outreach,* Vol. 1, No. 4, pages 351–516; October 2008.

The Evolution of Phototransduction and Eyes. *Philosophical Transactions of the Royal Society B,* Vol. 364, No. 1531, pages 2789–2967; October 12, 2009.

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CYBERSECURITY

HACKING THE LIGHTS OUT

Computer viruses have taken out hardened industrial control systems. The electrical power grid may be next

By David M. Nicol

IN BRIEF

Every facet of the modern electrical grid is controlled by computers. It is our greatest example of physical infrastructure interlinked with electronics.

The Stuxnet virus that infected Iran's nuclear program showed just how vulnerable machines could be to a well-crafted electronic virus.

The grid shares many of the vulnerabilities that Stuxnet exposed; being larger, its vulnerabilities are, if anything, more numerous.

Although a sophisticated attack could bring down a large chunk of the U.S. electrical grid, security is being ramped up.

VINCENT LAFORET *Redux Pictures*

LAST YEAR WORD BROKE OF A COMPUTER VIRUS THAT HAD managed to slip into Iran's highly secure nuclear enrichment facilities. Most viruses multiply without prejudice, but the Stuxnet virus had a specific target in its sights—one that is not connected to the Internet. Stuxnet was planted on a USB stick that was handed to an unsuspecting technician, who plugged it into a computer at a secure facility. Once inside, the virus spread silently for months, searching for a computer that was connected to a prosaic piece of machinery: a programmable logic controller, a special-purpose collection of microelectronics that commonly controls the cogs of industry—valves, gears, motors and switches. When Stuxnet identified its prey, it slipped in, unnoticed, and seized control.

The targeted controllers were attached to the centrifuges at the heart of Iran's nuclear ambitions. Thousands of these centrifuges are needed to process uranium ore into the highly enriched uranium needed to create a nuclear weapon. Under normal operating conditions, the centrifuges spin so fast that their outer edges travel just below the speed of sound. Stuxnet bumped this speed up to nearly 1,000 miles per hour, past the point where the rotor would likely fly apart, according to a December report by the Institute for Science and International Security. At the same time, Stuxnet sent false signals to control systems indicating that everything was normal. Although the total extent of the damage to Iran's nuclear program remains unclear, the report notes that Iran had to replace about 1,000 centrifuges at its Natanz enrichment facility in late 2009 or early 2010.

Stuxnet demonstrates the extent to which common industrial machines are vulnerable to the threat of electronic attack. The virus targeted and destroyed supposedly secure equipment while evading detection for months. It provides a dispiriting blueprint for how a rogue state or terrorist group might use similar technology against critical civilian infrastructure anywhere in the world.

Unfortunately, the electrical power grid is easier to break into than any nuclear enrichment facility. We may think of the grid as one gigantic circuit, but in truth the grid is made from thousands of components hundreds of miles apart acting in unerring coordination. The supply of power flowing into the grid must rise and fall in lockstep with demand. Generators must dole their energy out in precise coordination with the 60-cycle-per-second beat that the rest of the grid dances to. And while the failure of any single component will have limited repercussions to this vast circuit, a coordinated cyberattack on multiple

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points in the grid could damage equipment so extensively that our nation's ability to generate and deliver power would be severely compromised for weeks—perhaps even months.

Considering the size and complexity of the grid, a coordinated attack would probably require significant time and effort to mount. Stuxnet was perhaps the most advanced computer virus ever seen, leading to speculation that it was the work of either the Israeli or U.S. intelligence agencies—or both. But Stuxnet's code is now available on the Internet, raising the chance that a rogue group could customize it for an attack on a new target. A less technologically sophisticated group such as al Qaeda probably does not have the expertise to inflict significant damage to the grid at the moment, but black hat hackers for hire in China or the former Soviet Union might. It is beyond time we secured the country's power supply.

THE BREAK-IN

A YEAR AGO I TOOK PART in a test exercise that centered on a fictitious cyberattack on the grid. Participants included representatives from utility companies, U.S. government agencies and the military. (Military bases rely on power from the commercial grid, a fact that has not escaped the Pentagon's notice.) In the test scenario, malicious agents hacked into a number of transmission substations, knocking out the specialized and expensive devices that ensure voltage stays constant as electricity flows across long high-power transmission lines. By the end of the exercise half a dozen devices had been destroyed, depriving power to an entire Western state for several weeks.

Computers control the grid's mechanical devices at every level, from massive generators fed by fossil fuels or uranium all the way down to the transmission lines on your street. Most of these computers use common operating systems such as Windows and Linux, which makes them as vulnerable to malware as your desktop PC is. Attack code such as Stuxnet is successful for three main reasons: these operating systems implicitly trust running software to be legitimate; they often have flaws that admit penetration by a rogue program; and industrial settings often do not allow for the use of readily available defenses.

Even knowing all this, the average control system engineer would have once dismissed out of hand the possibility of remotely launched malware getting close to critical controllers, arguing that the system is not directly connected to the Internet. Then Stuxnet showed that control networks with no permanent connection to anything else are still vulnerable. Malware can piggyback on a USB stick that technicians plug into the control system, for example. When it comes to critical electronic circuits, even the smallest back door can let an enterprising burglar in.

Consider the case of a transmission substation, a waypoint on electricity's journey from power plant to your home. Substations take in high-voltage electricity coming from one or more power plants, reduce the voltage and split the power into multiple output lines for local distribution. A circuit breaker guards each of these lines, standing ready to cut power in case of a fault. When one output line's breaker trips, all of the power it would have carried flows to the remaining lines. It is not hard to see that if all the lines are carrying power close to their capacity,

MARK DUNCAN *AP Photo* (*left*); MARK PETERSON *Redux Pictures* (*center*); EBRAHIM NOROUZI *AP Photo* (*right*)

TIMELINE

Digital Attacks, Physical Harm

As industrial machinery goes online, the potential for wreaking havoc grows. Intrusions over the past decade show that the grid is not the only vulnerability—anything with a microchip can be a target.

Davis-Besse nuclear plant

April 2000
A disgruntled former employee of a water treatment firm uses stolen radio parts to issue faulty commands to sewage equipment in Queensland, Australia, causing more than 200,000 gallons of raw sewage to spill into local parks and rivers.

January 2003
The Slammer worm bypasses multiple firewalls to infect the operations center at Ohio's Davis-Besse nuclear power plant. The worm spreads from a contractor's computer into the business network, where it jumps to the computers controlling plant operations, crashing multiple safety systems. The plant was off-line at the time.

March 2007
Government officials simulate a cyberattack on electricity generation equipment at the Idaho National Laboratory. A video of the test, called Aurora, is later leaked to CNN.

2000 2001 2002 2003 2004 2005

then a cyberattack that trips out half of the output lines and keeps the remaining ones in the circuit may overload them.

These circuit breakers have historically been controlled by devices connected to telephone modems so that technicians can dial in. It is not difficult to find those numbers; hackers invented programs 30 years ago to dial up all phone numbers within an exchange and make note of the ones to which modems respond. Modems in substations often have a unique message in their dial-up response that reveals their function. Coupled with weak means of authentication (such as well-known passwords or no passwords at all), an attacker can use these modems to break into a substation's network. From there it may be possible to change device configurations so that a danger condition that would otherwise open a circuit breaker to protect equipment gets ignored.

New systems are not necessarily more secure than modems. Increasingly, new devices deployed in substations may communicate with one another via low-powered radio, which does not stop at the boundaries of the substation. An attacker can reach the network simply by hiding in nearby bushes with his computer. Encrypted Wi-Fi networks are more secure, but a sophisticated attacker can still crack their encryption using readily available software tools. From here he can execute a man-in-the-middle attack that causes all communication between two legitimate devices to pass through his computer or fool other devices into accepting his computer as legitimate. He can craft malicious control messages that hijack the circuit breakers—tripping a carefully chosen few to overload the other lines perhaps or making sure they do not trip in an emergency.

Once an intruder or malware sneaks in through the back door, its first step is usually to spread as widely as possible. Stuxnet again illustrates some of the well-known strategies. It proliferated by using an operating system mechanism called autoexec. Windows computers read and execute the file named AUTOEXEC.BAT every time a new user logs in. Typically the program locates printer drivers, runs a virus scan or performs other basic functions. Yet Windows assumes that any program with the right name is trusted code. Hackers thus find ways to alter the AUTOEXEC.BAT file so that it runs the attackers' code.

Attackers can also use clever methods that exploit the economics of the power industry. Because of deregulation, competing utilities share responsibility for grid operation. Power is generated, transmitted and distributed under contracts obtained in online auctions. These markets operate at multiple timescales—one market might trade energy for immediate delivery and another for tomorrow's needs. A utility's business unit must have a constant flow of real-time information from its operations unit to make smart trades. (And vice versa: operations need to know how much power they need to produce to fulfill the business unit's orders.) Here the vulnerability lies. An enterprising hacker might break into the business network, ferret out user names and passwords, and use these stolen identities to access the operations network.

Other attacks might spread by exploiting the small programs called scripts that come embedded in files. These scripts are ubiquitous—PDF files routinely contain scripts that aid in file display, for example—but they are also a potential danger. One computer security company recently estimated that more than 60 percent of all targeted attacks use scripts buried in PDF files. Simply reading a corrupted file may admit an attacker onto your computer.

Consider the hypothetical case where a would-be grid attacker first penetrates the Web site of a software vendor and replaces an online manual with a malicious one that appears exactly like the first. The cyberattacker then sends an engineer at the power plant a forged e-mail that tricks the engineer into fetching and opening the booby-trapped manual. Just by going online to download an updated software manual, the unwitting engineer opens his power plant's gates to the Trojan horse. Once inside, the attack begins.

SEARCH AND DESTROY

AN INTRUDER on a control network can issue commands with potentially devastating results. In 2007 the Department of Homeland Security staged a cyberattack code-named Aurora at the Idaho National Laboratory. During the exercise, a researcher posing as a malicious hacker burrowed his way into a network connected to a medium-size power generator. Like all generators, it creates alternating current operating at almost exactly 60 cycles per second. In every cycle, the flow of electrons starts out moving in one direction, reverses course, and then returns to its original state. The generator has to be moving electrons in exactly the same direction at exactly the same time as the rest of the grid.

During the Aurora attack, our hacker issued a rapid succession of on/off commands to the circuit breakers of a test generator at the laboratory. This pushed it out of sync with the power grid's own oscillations. The grid pulled one way, the generator another. In effect, the generator's mechanical inertia fought the grid's electrical inertia. The generator lost. Declassified video shows the hulking steel machine shuddering as though a train hit the building. Seconds later steam and smoke fill the room.

Industrial systems can also fail when they are pushed beyond their limits—when centrifuges spin too fast, they disintegrate. Similarly, an attacker could make an electric generator produce a surge of power that exceeds the limit of what the transmission lines can carry. Excess power would then have to escape as heat. Enough excess over a long enough period causes the line to sag and eventually to melt. If the sagging line comes

January 2008
A senior CIA official reveals that hackers have frequently infiltrated electric utilities outside the U.S. and made extortion demands. In at least one case, the hackers were able to shut off the power supply to several (unnamed) cities.

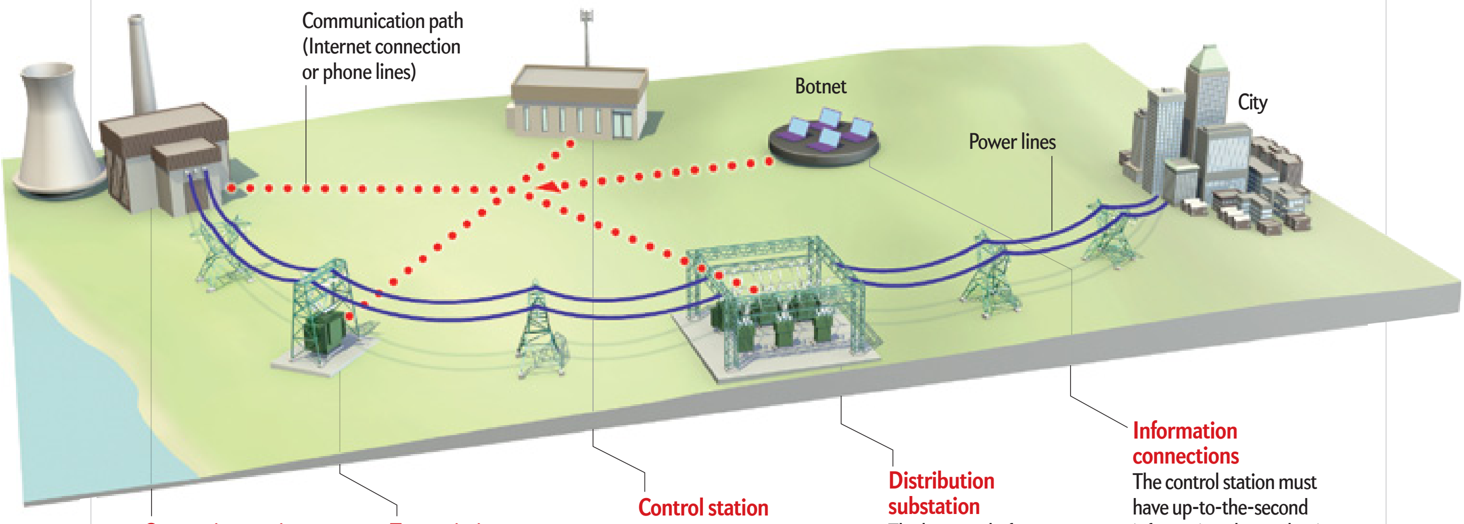
April 2009
The *Wall Street Journal* reports that cyberspies from "China, Russia and other countries" have penetrated the U.S. electrical power grid and left behind software that could be used to disrupt the system.

October 2010
Security officials in Iran, Indonesia and elsewhere report the discovery of the Stuxnet virus, a piece of malware designed specifically to interfere with industrial control systems made by Siemens.

2006 2007 2008 2009 2010 2011

Holes in the Grid

The modern electrical grid involves an intricate balance between the amount of energy needed by society and the amount generated at power plants. Dozens of components orchestrate the flow of electrons over distances of hundreds of miles, aligning the alternating currents and making sure no single component gets stretched beyond its limits. Any one of these parts might suffer from the attention of malicious actors. Here are some of the most troublesome choke points and the ways they might be compromised.



Generating station
It does not matter if the fuel is coal, uranium or even solar—electricity going into the U.S. power grid must alternate at 60 cycles a second, and it must enter perfectly aligned with the rhythm of the rest of the grid. An attacker might send instructions to a generator that throws its output off by a half-step, the electrical equivalent of throwing your car into reverse while heading down the highway at 50 miles per hour. The generator—like your car's transmission—will end up a smoking heap.

Transmission substation
Electricity coming out of generating stations comes at very high voltages—the better to avoid losses from electrical resistance en route. Transmission substations are the first step in bringing this voltage down. Many older stations have dial-up modems so that technicians can dial in and perform maintenance. Hackers can use these devices to access and change critical settings.

Control station
The grid's nerve centers, control stations monitor conditions throughout. They are also where supply meets demand. When demand goes up, prices follow, and a utility might activate more power capacity to provide additional supplies. Although the operations center of a control station is not supposed to be connected to the Internet, its business center must be. A hacker might burrow into the business side and use links between that side and operations to infect critical control systems.

Distribution substation
The last step before electricity goes into homes or businesses, these substations might combine power coming in from a few different power stations and send it out on dozens or hundreds of smaller lines. Newer stations might be equipped with wireless communications equipment—either radio signals or Wi-Fi. An intruder who hides just outside a station's walls could intercept traffic and mimic legitimate instructions.

Information connections
The control station must have up-to-the-second information about what is going on at every step of the process for technicians to make smart decisions about what to do next. Hackers with access to thousands of ordinary computers—a so-called botnet—could direct these machines to send messages that interrupt the flow of ordinary network traffic. Such a denial-of-service attack would mean that control operators would be making decisions based on old information—something akin to driving a car using the information you had 10 seconds ago.

into contact with anything—a tree, a billboard, a house—it could create a massive short circuit.

Protection relays typically prevent these shorts, but a cyberattack could interfere with the working of the relays, which means damage would be done. Furthermore, a cyberattack could also alter the information going to the control station, keeping operators from knowing that anything is amiss. We have all seen the movies where crooks send a false video feed to a guard.

Control stations are also vulnerable to attack. These are command and control rooms with huge displays, like the war room in *Dr. Strangelove*. Control station operators use the displays to monitor data gathered from the substations, then issue commands to change substation control settings. Often these stations are responsible for monitoring hundreds of substations spread over a good part of a state.

Data communications between the control station and substations use specialized protocols that themselves may have vulnerabilities. If an intruder succeeds in launching a man-in-the-middle attack, that individual can insert a message into an exchange (or corrupt an existing message) that causes one or both of the computers at either end to fail. An attacker can also try just injecting a properly formatted message that is out of context—a digital non sequitur that crashes the machine.

Attackers could also simply attempt to delay messages trav-

Illustration by George Retseck

eling between control stations and the substations. Ordinarily the lag time between a substation's measurement of electricity flow and the control station's use of the data to adjust flows is small—otherwise it would be like driving a car and seeing only where you were 10 seconds ago. (This kind of lack of situational awareness was a contributor to the Northeast Blackout of 2003.)

Many of these attacks do not require fancy software such as Stuxnet but merely the standard hacker's tool kit. For instance, hackers frequently take command over networks of thousands or even millions of ordinary PCs (a botnet), which they then instruct to do their bidding. The simplest type of botnet attack is to flood an ordinary Web site with bogus messages, blocking or slowing the ordinary flow of information. These "denial of service" attacks could also be used to slow traffic moving between the control station and substations.

Botnets could also take root in the substation computers themselves. At one point in 2009 the Conficker botnet had insinuated itself into 10 million computers; the individuals, as yet unknown, who control it could have ordered it to erase the hard drives of every computer in the network, on command. A botnet such as Conficker could establish itself within substations and then have its controller direct them simultaneously to do anything at any time. According to a 2004 study by researchers at Pennsylvania State University and the National Renewable Energy Laboratory in Golden, Colo., an attack that incapacitated a carefully chosen minority of all transmission substations—about 2 percent, or 200 in total—would bring down 60 percent of the grid. Losing 8 percent would trigger a nationwide blackout.

WHAT TO DO

WHEN MICROSOFT LEARNS of a potential security liability in its Windows software, it typically releases a software patch. Individual users and IT departments the world over download the patch, update their software and protect themselves from the threat. Unfortunately, things are not that simple on the grid.

Whereas the power grid uses the same type of off-the-shelf hardware and software as the rest of the world, IT managers at power stations cannot simply patch the faulty software when bugs crop up. Grid control systems cannot come down for three hours every week for maintenance; they have to run continuously. Grid operators also have a deep-rooted institutional conservatism. Control networks have been in place for a long time, and operators are familiar and comfortable with how they work. They tend to avoid anything that threatens availability or might interfere with ordinary operations.

In the face of a clear and present danger, the North American Electric Reliability Corporation (NERC), an umbrella body of grid operators, has devised a set of standards designed to protect critical infrastructure. Utilities are now required to identify their critical assets and demonstrate to NERC-appointed auditors that they can protect them from unauthorized access.

Yet security audits, like financial audits, cannot possibly be exhaustive. When an audit does go into technical details, it does so only selectively. Compliance is in the eye of the auditor.

The most common protection strategy is to employ an electronic security perimeter, a kind of cybersecurity Maginot line. The first line of defense is a firewall, a device through which all electronic messages pass. Each message has a header indicating where it came from, where it is going, and what protocol is used to interpret the message. Based on this information, the firewall allows some messages through and stops others. An auditor's job is partly to make sure the firewalls in a utility are configured properly so that they do not let any unwanted traffic in or out. Typically the auditors would identify a few critical assets, get a hold of the firewall configuration files, and attempt to sort through by hand the ways in which a hacker might be able to break through the firewall.

Firewalls, though, are so complex that it is difficult for an auditor to parse all the myriad possibilities. Automated software tools might help. Our team at the University of Illinois at Urbana-Champaign has developed the Network Access Policy Tool, which is just now being used by utilities and assessment teams. The software needs only a utility's firewall configuration files—it does not even have to connect to the network. Already it has found a number of unknown or long-forgotten pathways that attackers might have exploited.

The DOE has come out with a roadmap that lays out a strategy for enhancing grid security by 2015. (A revision due this year extends this deadline to 2020.) One focus: creating a system that recognizes an intrusion attempt and reacts to it automatically. That would block a Stuxnet-like virus as soon as it jumped from the USB stick. But how can an operating system know which programs are to be trusted?

One solution is to use a one-way hash function, a cryptographic technique. A hash function takes a fantastically huge number—for example, all the millions of 1s and 0s of a computer program, expressed as a number—and converts it to a much smaller number, which acts as a signature. Because programs are so large, it is highly unlikely that two different ones would result in the same signature value. Imagine that every program that wants to run on a system must first go through the hash function. Its signature then gets checked against a master list; if it does not check out, the attack stops there.

The DOE also recommends other security measures, such as physical security checks at operator workstations (think radio chips in identification badges). It also highlights the need to exert tighter control over communication between devices inside the network. The 2007 Aurora demonstration involved a rogue device tricking a generator's network into believing it was sending authoritative commands. These commands eventually led to the destruction of the generator.

These worthwhile steps will require time and money and effort. If we are going to achieve the DOE roadmap to a more secure grid in the next decade, we are going to have to pick up the pace. Let us hope we have even that much time. SA

MORE TO EXPLORE

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Security of Critical Control Systems Sparks Concern. David Geer in *IEEE Computer,* Vol. 39, No. 1, pages 20–23; January 2006.

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SCIENTIFIC AMERICAN ONLINE
For an extended look at the history of electronic attacks on physical structures, visit ScientificAmerican.com/jul2011/lights-out


John R. Carlson is a professor of molecular, cellular and developmental biology at Yale University. He has studied the molecular and cellular basis of insect olfaction for 25 years.


Allison F. Carey recently graduated from Yale with an M.D. and a doctorate in neuroscience. She is continuing her research on malaria at the Pasteur Institute in Paris.

DISEASE CONTROL

SCENT OF A HUMAN

Decoding how a mosquito sniffs out human targets could lead to better traps and repellents that cut malaria's spread

By John R. Carlson and Allison F. Carey

MOSQUITOES HAVE REMARKABLY REFINED POWERS OF SMELL. The insects that spread malaria across sub-Saharan Africa come exquisitely equipped to find human blood. They home in on the scent of human breath and sweat and swiftly insert their needlelike mouthparts into the target's skin. As they dine, their saliva transmits the malaria parasite into the wound. With a simple bite, they can ultimately take a life.

Other mosquitoes prefer different species—say, cattle or birds. Some, it seems, even favor selected individuals within the target group; certain people at a summer barbeque will be attacked relentlessly, yet others will remain unbitten. And some mosquitoes can identify their victims from more than 165 feet.

If investigators could better understand how the mosquito olfactory system works—how it manages to detect exactly the suite of volatile chemicals unique to its favored source of blood—they should be able to devise new, more effective ways of masking those scents or "jamming" the insects' olfactory "radar" to prevent bites. In the developed world, such bites are often just a nuisance, but in Africa and elsewhere they cause nearly a million deaths a year from malaria alone.

We are among the many researchers determined to fight malaria's spread. To our delight, we have recently made exciting strides in deciphering how the mosquito *Anopheles gambiae,* the main carrier of malaria parasites, detects the scent of its human victims. The findings are now pointing to ideas for repellents and traps that could complement other defensive measures such as bed nets and, one day, an effective vaccine.

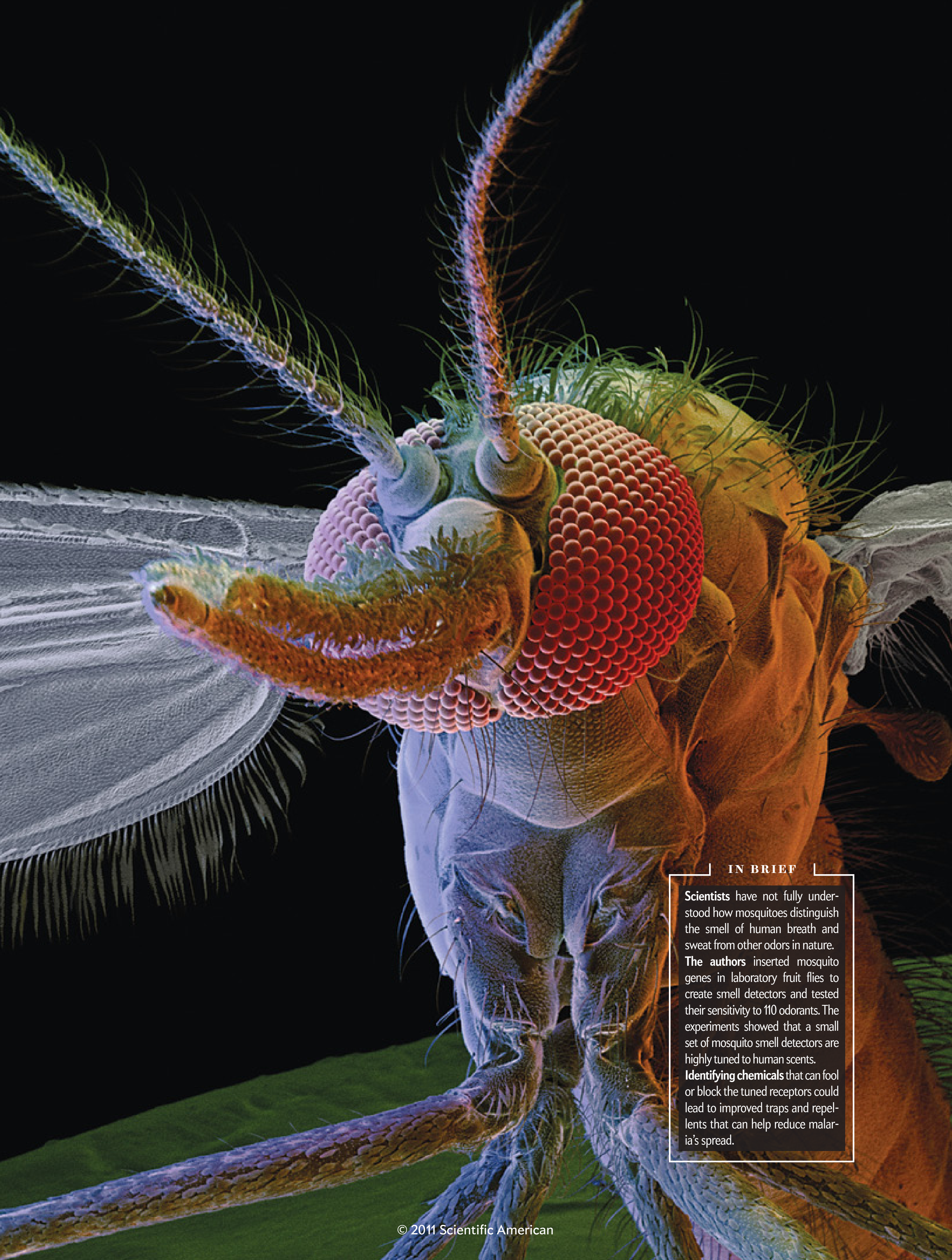
GENES FOR ODORS

TO INVESTIGATE HOW malaria-causing mosquitoes detect their human prey, we began with a different insect, the fruit fly *Drosophila melanogaster.* Unlike mosquitoes, fruit flies breed quickly and are easy to maintain in a laboratory, and their genes can be readily manipulated. *D. melanogaster* has become a lab workhorse, so we use it to reveal the basic cellular and molecular mechanisms of insect olfaction, knowledge we can then apply in more difficult experiments with less tractable mosquitoes.

Fruit flies, like mosquitoes, detect odors with antennae and maxillary palpi, organs that protrude from the head and act as a nose. Tiny bristles that cover these protrusions encase the ends of excitable nerve cells dedicated to smell. Odorant molecules slip through pores in the bristles to reach odor-detecting molecules, or receptors, inside. When receptors bind to odor molecules, an electrical signal travels down the nerve cell, or neuron, to the insect's brain, indicating that the odor is present.

For years we and others had tried unsuccessfully to find the genes for insect odorant receptors, hoping to learn exactly how the creatures distinguish among the countless odorants in the environment. Breakthroughs finally began coming in 1999. Researchers on our team at Yale University and elsewhere discov-

DAVID SCHARF



IN BRIEF

Scientists have not fully understood how mosquitoes distinguish the smell of human breath and sweat from other odors in nature.

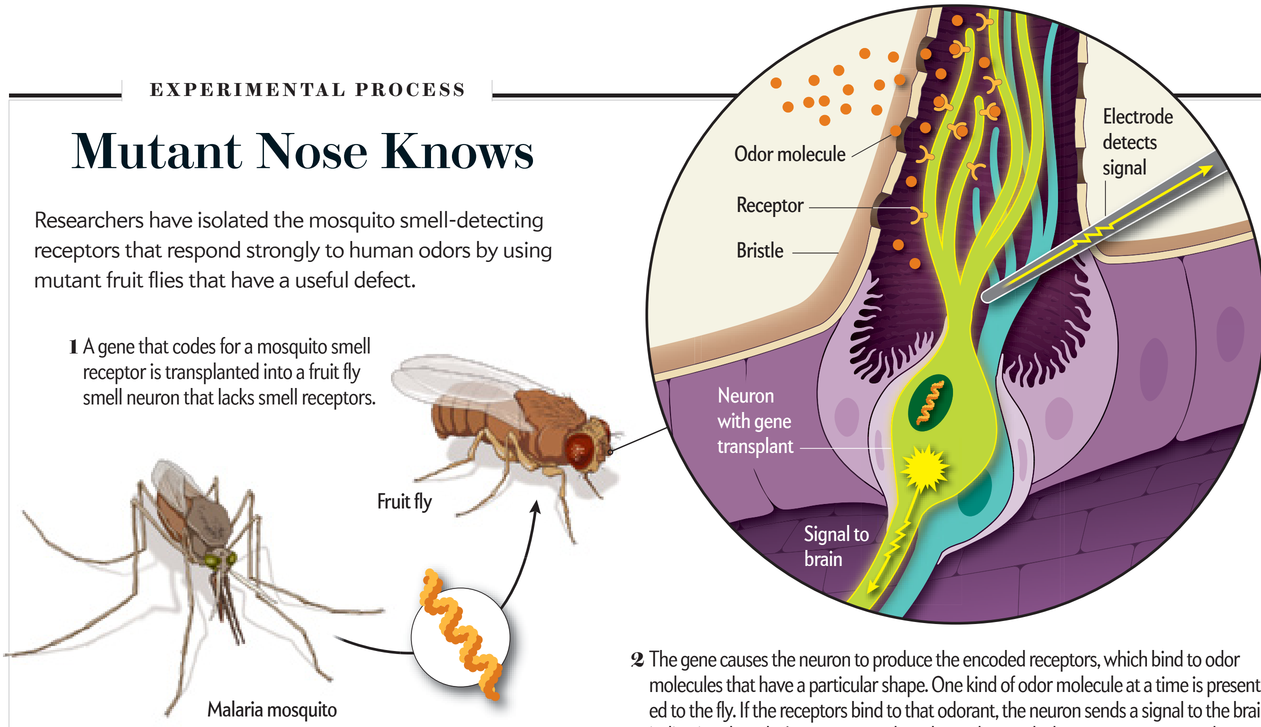
The authors inserted mosquito genes in laboratory fruit flies to create smell detectors and tested their sensitivity to 110 odorants. The experiments showed that a small set of mosquito smell detectors are highly tuned to human scents.

Identifying chemicals that can fool or block the tuned receptors could lead to improved traps and repellents that can help reduce malaria's spread.

EXPERIMENTAL PROCESS

Mutant Nose Knows

Researchers have isolated the mosquito smell-detecting receptors that respond strongly to human odors by using mutant fruit flies that have a useful defect.



2 The gene causes the neuron to produce the encoded receptors, which bind to odor molecules that have a particular shape. One kind of odor molecule at a time is presented to the fly. If the receptors bind to that odorant, the neuron sends a signal to the brain indicating the odor's presence, and an electrode reveals the response to researchers.

ered the first genes coding for the receptors. Over time we found 60 odorant receptor genes in the fruit fly. Knowing the sequence of their DNA code opened the door to figuring out how the receptors work. We also found that the genetics of the olfactory systems of the fruit fly and the mosquito are similar, so studying the fly would help us understand olfaction in the mosquito.

A key insight came from a genetic mutant of *D. melanogaster* that arrived in our lab serendipitously. In November 2001 one of us (Carlson) gave a seminar at Brandeis University near Boston. The seminar was about *Or22a,* the first fruit fly odorant receptor gene that our lab had discovered. After the talk, an assistant professor at Brandeis came up to the podium and said that he happened to have a mutant *D. melanogaster* strain that was missing the gene encoding this odorant receptor. He asked if the mutant might be useful. It took Carlson about a millisecond to respond, "Yes!" The next day Carlson drove a small vial of the mutant flies down Interstate 91 to our Yale facility in New Haven, Conn.

A major goal was to determine which fruit fly receptors responded to which odorants. A single neuron has thousands of receptors, but they are identical; each type binds only a small subset of odor molecules. Different neurons have different types of receptors that bind to other subsets. Because the mutant fruit flies were missing one particular odorant receptor gene, we hypothesized that they would harbor a kind of receptorless, or "empty," neuron.

Sure enough, they did. Applying sophisticated genetic techniques developed to study *D. melanogaster,* we inserted a fruit fly receptor gene into this neuron, which then produced the encoded receptor molecules. For each receptor, we could then determine which odorants activated it. By systematically fitting each *D. melanogaster* odorant receptor into an empty neuron, one at a time, and exposing the neuron to a variety of odoriferous compounds, we could learn which of those chemicals generated a response for each of the insect's many receptors.

Over the next three years Elissa Hallem, then a graduate student at Yale, did just that. She found that individual receptors responded to a limited subset of odorants and that individual odorants activate subsets of receptors. Similar results have been observed in the mammalian olfactory system. Thus, animals, from fruit flies to humans, detect scents in the same way: different odors activate different combinations of receptors. This strategy helps to explain how animals, including mosquitoes, can discriminate among the vast number of smells found in nature without having to possess a receptor dedicated to every single variety.

A FLY THAT SNIFFS LIKE A MOSQUITO

HAVING CHARACTERIZED the fruit fly's odorant receptor genes, we wanted to try to insert receptor genes from the malaria-carrying mosquito into the fly's empty neuron. In collaboration with Laurence J. Zwiebel of Vanderbilt University, Hugh M. Robertson of the University of Illinois at Urbana-Champaign and their colleagues, we had identified a family of 79 genes likely to be odorant receptor genes in *A. gambiae* by searching for sequences of DNA similar to those in the fruit fly's receptor genes. Transplanting any one of the genes into a fruit fly's empty neuron could theoretically produce a mosquito odorant receptor in the fly. But the experiment could easily fail. The two insect species are separated by 250 million years of evolution. We had no idea if a mosquito receptor gene would function in a fruit fly neuron.

Our experimental system is attached to a loudspeaker, so if an olfactory neuron fires, our electrode senses it and the speaker generates a staccato series of clicks. When we tested a series of odorants on the first empty fly neuron that had been fitted with a mosquito gene, the loudspeaker remained disappointingly silent. We suspected that the mosquito receptor might not work in the fruit fly neuron. But Hallem continued testing samples. When she reached a compound called 4-methylphenol, the loudspeaker began screaming, and we were equally excited. We later learned that

Illustration by Tommy Moorman

4-methylphenol, which smells a bit like used gym socks, is a component of human sweat. We had found a way to decode which odorants elicit a response from which mosquito receptors, information that could help us understand how mosquitoes locate their human prey and how we might interfere with that process.

With this encouraging result in hand, we read widely about human odorants and selected 110 compounds to test, including many that are components of human sweat. We included odorants with diverse molecular structures, creating a broad sample. One by one, we began transplanting each of the 79 possible *A. gambiae* receptor genes into empty neurons. Fifty of the receptor molecules proved functional in our setup. We then began testing the panel of 110 odorants against the 50 functional receptors, producing 5,500 odorant receptor combinations. The extensive sampling required many long days and nights.

From this data set, we identified several receptors that responded strongly to only one or a very few compounds. We were interested in these "narrowly tuned" receptors. We reasoned that if a mosquito needed to detect a particular compound with a high degree of sensitivity and specificity—notably one that signals a source of blood—the mosquito might use a dedicated receptor. Indeed, we found that most of the narrowly tuned receptors responded to components of human sweat. For example, the first mosquito receptor Hallem had tested in the empty neuron—the receptor that responded so strongly to 4-methylphenol—turned out to be narrowly tuned. Out of the 110 compounds, only a few others excited that receptor as strongly. Another receptor was narrowly tuned to 1-octen-3-ol, common in human and animal odor. It strongly attracts several mosquito species, including *Culex pipiens,* the one that is commonly found in U.S. backyards and that can carry West Nile virus. Some commercial traps sold to lure mosquitoes away from people in backyards emit 1-octen-3-ol.

JAM THE NERVES, STOP THE INSECTS

OUR RESULTS could speed development of better mosquito repellents and traps. One standard method for testing compounds involves putting substances into traps in the field to see whether they attract mosquitoes. But because the process is slow, only a limited number of chemicals can be tested. Classical lab experiments also have drawbacks. In many cases, human volunteers allow an arm to be coated with a compound, and then they insert the arm into a clear box containing dozens of mosquitoes; chemicals that deter the insects may later be pursued as repellents. In our approach, we can rapidly examine many more chemicals, making discovery of new, more effective lures or repellents much more likely—and without human subjects.

Vanderbilt's Zwiebel, for instance, is using *A. gambiae* odorant receptors grown in cells in small lab dishes. Robots expose the cells to thousands of compounds in just a few hours. So far Zwiebel has screened more than 200,000 compounds, and more than 400 of them have activated or inhibited the odorant receptors. These compounds will be analyzed further in experiments, and the best of them will advance to field tests.

The lab approach also allows us to screen for compounds that act as "superactivators"—ones that jam olfactory neurons by overexciting them to the point that their signaling either shuts down or confuses the mosquito's brain. "Confusant" compounds could be released near the huts in which villagers in sub-Saharan Africa sleep, preventing malaria-carrying mosquitoes from finding the inhabitants. Lab screening could also identify compounds that inhibit the narrowly tuned receptors, blocking the insect's ability to sense a target. These masking agents, too, could be released at huts or used in repellents applied to the skin, to prevent mosquitoes from realizing that they were near a source of blood. Compounds that mosquitoes find offensive might also be identified for repellents. Our collaborators at Wageningen University in the Netherlands are experimenting with *A. gambiae* mosquitoes to determine whether blends of some of the compounds we have identified may be useful in these ways. Our colleagues have already found some powerful combinations.

Historically many methods of insect control, such as the widespread spraying of the insecticide DDT, have harmed animals and perhaps people. Olfactory-based control methods can be far less damaging. An olfactory trap requires only a small amount of attractant because mosquitoes are so sensitive to these cues. Attractive compounds that are commonly found in human sweat and breath should be nontoxic in low doses, too. If poisons were also used in these traps, they would be contained instead of distributed broadly. Moreover, olfactory-based insect control could be much more precise than that based on insecticides. Comparisons of our data from mosquitoes and fruit flies show that most of the narrowly tuned receptors of *A. gambiae* respond to compounds found in human sweat, whereas the narrowly tuned receptors of *D. melanogaster* respond to volatiles emitted by fruit. Blends of attractants can be chosen that preferentially lure the target insect, leaving a much lighter mark on the environment. Overall, olfactory-based insect control should be much less damaging to the natural world and more politically acceptable than the blanket spraying of poisons. And if a cocktail of effective compounds can be used instead of a single compound, resistance is less likely to arise in mosquito populations.

For the agents discovered by our methods to be useful in poverty-stricken nations, they would have to be packaged inexpensively. Traps that release carbon dioxide from compressed gas tanks—used widely in rich countries—are impractical in rural areas of the developing world. Attractant and repellent compounds must also be chemically stable in blistering tropical heat. Whether those demands can be met remains to be seen.

A multifaceted approach is needed to eradicate malaria. Bed nets and improved drugs will play a major role. Researchers are steadfastly trying to develop an effective vaccine. Still, the need for additional tools in the antimalaria armament is pressing. Precisely manipulating olfactory-guided mosquito behavior could be a big step. In the struggle against a disease that affects hundreds of millions of people every year, even a small contribution could make a large difference in the lives of many. SA

MORE TO EXPLORE

Olfactory Regulation of Mosquito-Host Interactions. Lawrence J. Zwiebel and W. Takken in *Insect Biochemistry and Molecular Biology,* Vol. 34, No. 7, pages 645–652; July 2004.

Insects as Chemosensors of Humans and Crops. Wynand van der Goes van Naters and John R. Carlson in *Nature,* Vol. 444, pages 302–307; November 16, 2006.

Odorant Reception in the Malaria Mosquito *Anopheles gambiae.* Allison F. Carey et al. in *Nature,* Vol. 464, pages 66–71; March 4, 2010.

World Health Organization malaria page: **www.who.int/topics/malaria/en**

SCIENTIFIC AMERICAN ONLINE
For scanning electron microscope images of mosquito and fruit fly smell organs, go to **ScientificAmerican.com/jul2011/carlson**

COSMOLOGY

Bad Boy of Physics

Leonard Susskind rebelled as a teen and never stopped. Today he insists that reality may forever be beyond reach of our understanding

Interview by Peter Byrne

STANFORD UNIVERSITY PHYSICIST LEONARD SUSSKIND REVELS IN DISCOVERING IDEAS that transform the status quo in physics. Forty years ago he co-founded string theory, which was initially derided but eventually became the leading candidate for a unified theory of nature. For years he disputed Stephen Hawking's conjecture that black holes do not merely swallow objects but grind them up beyond recovery, in violation of quantum mechanics. Hawking eventually conceded. And he helped to develop the modern conception of parallel universes, based on what he dubbed the "landscape" of string theory. It spoiled physicists' dream to explain the universe as the unique outcome of basic principles.

Physicists seeking to understand the deepest levels of reality now work within a framework largely of Susskind's making. But a funny thing has happened along the way. Susskind now wonders whether physicists *can* understand reality.

Susskind worries that reality might be beyond our limited capacity to visualize it. He is not the first to express such a concern. In the 1920s and 1930s the founders of quantum mechanics split into realist and antirealist camps. Albert Einstein and other realists held that the whole point of physics is to come up with some mental picture, however imperfect, of what objective reality is. Antirealists such as Niels Bohr said those mental images are fraught with peril; scientists should confine themselves to making and testing empirical predictions. Susskind thinks the contradictions and paradoxes of modern physics vindicate Bohr's wariness.

One thing that led Susskind to this conclusion is his principle of black hole complementarity, which holds that there is an inherent ambiguity in the fate of objects that fall into a black hole. From the point of view of the falling object itself, it passes without incident through the hole's perimeter, or ho-

IN BRIEF

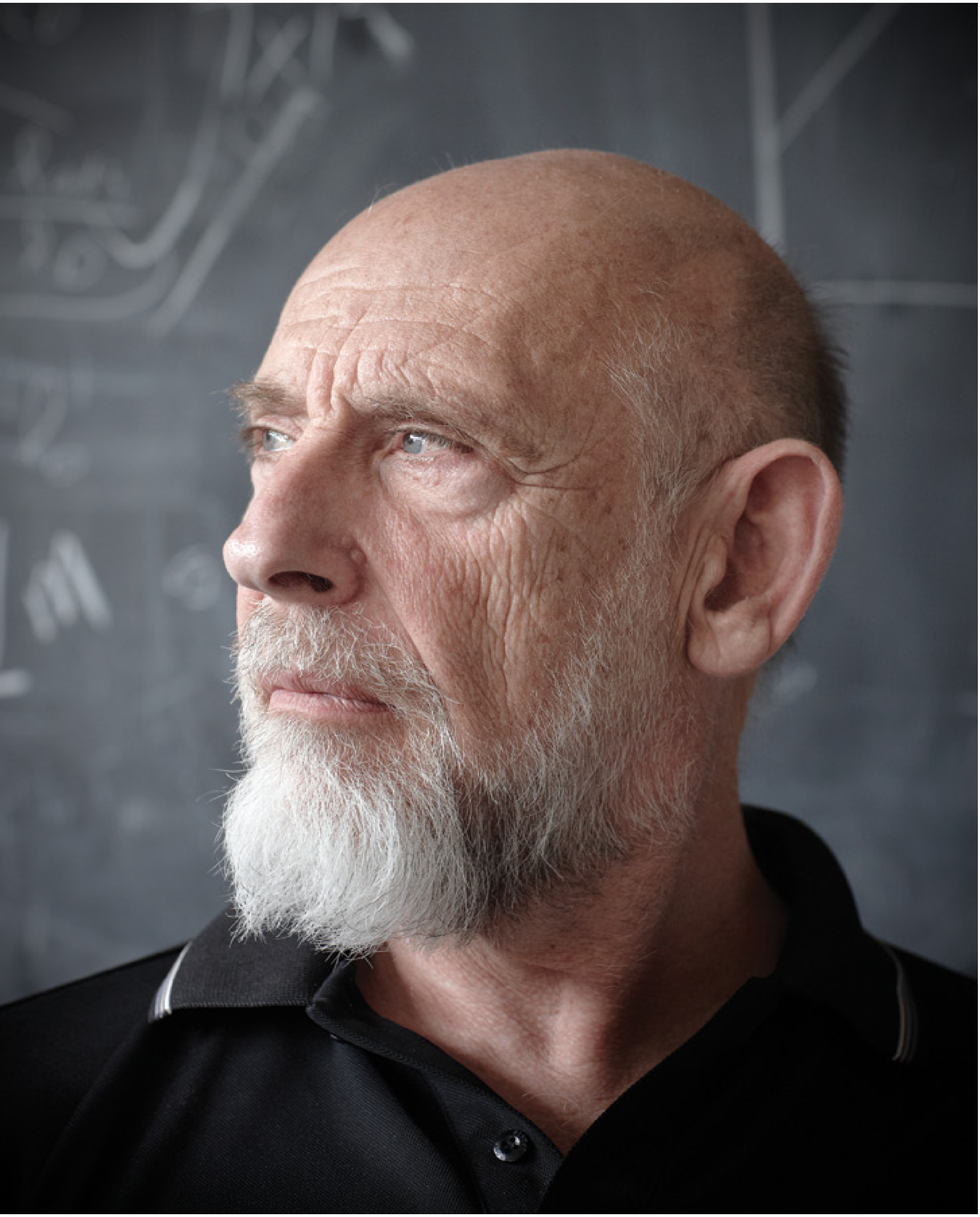
WHO
LEONARD SUSSKIND

VOCATION | AVOCATION
Theoretical physicist, known especially for pioneering string theory, black hole physics and the multiverse

WHERE
Stanford University

RESEARCH FOCUS
What is the deep nature of physical reality?

BIG PICTURE
We may never be able to grasp that reality. The universe and its ingredients may be impossible to describe unambiguously.



Photograph by Timothy Archibald

rizon, and is destroyed when it reaches the hole's center, or singularity. But from the vantage point of an external observer, the falling object is incinerated at the horizon. So what really happens? The question, according to the principle of black hole complementarity, is meaningless: both interpretations are valid.

A related idea favoring antirealism is the holographic principle that Susskind and Nobel laureate Gerard 't Hooft of Utrecht University formulated in the mid-1990s. It holds that what happens in any volume of spacetime can be explained by what happens on its boundary. Although we usually think of objects as zipping around three-dimensional space, we can equally well think of them as flattened blobs sliding across a two-dimensional surface. So which is the true reality: the boundary or the interior? The theory does not say. Reality, in this holographic conjecture, is perspectival.

Hoping to better understand how the tension between hard evidence and unproved conjecture works at the frontier of physics, we asked Susskind to explain how his ideas have evolved.

Scientific American: How did the son of a Bronx plumber end up questioning the nature of reality?

LEONARD SUSSKIND: I was a bad high school student. I was very good in mathematics, but I was a bad boy, and I got in trouble a lot. The effect of that is I wasn't allowed to take regular physics. I was told I had to take automotive physics. But then in college, which was an engineering school, I took my first physics course. I was just so much better than anybody else, including the professor. And fortunately, it was not a source of contention between us that I could do the things he couldn't. But then I was actually told by one of the engineering professors that he didn't think I was cut out to be an engineer, which was correct. I asked him, "What should I do?" He said, "Well, you're exceptionally smart. You should become a scientist."

Did you take any philosophy courses?

Yeah, I did in college. I was quite fascinated by some of the concepts. My interest in it lapsed when I really got hooked by physics.

Are there any philosophers of science whom you like?

I'm one of the few physicists I know who likes Thomas Kuhn. He was partly a historian of science, partly a sociologist. He got the basic idea right of what happens when the scientific paradigm shifts. A radical change of perspective suddenly occurs. Wholly new ideas, concepts, abstractions and pictures become relevant. Relativity was a big paradigm shift. Quantum mechanics was a big paradigm shift. So we keep on inventing new realisms. They never completely replace the old ideas, but they do largely replace them with concepts that work better, that describe nature better, that are often very unfamiliar, that make people question what is meant by "reality." Then the next thing comes along and turns that on its head. And we are always surprised that the old ways of thinking, the wiring that we have or the mathematical wiring that we may have created, simply fail us.

In the midst of all this remodeling, is there room for such a thing as an objective reality?

Every physicist must have some sense that there are objective things in the world and that it's our job to go and find out what those objective things are. I don't think you could do that without having a sense that there is an objective reality. The evidence for objectivity is that experiments are reproducible. If you kick a rock once, you'll hurt your toe. If you kick a rock twice, you'll hurt your toe twice. Do the same experiment over and over with a rock, and you'll reproduce the same effect.

That said, physicists almost never talk about reality. The problem is that what people tend to mean by "reality" has more to do with biology and evolution and with our hardwiring and our neural architecture than it has to do with physics itself. We're prisoners of our own neural architecture. We can visualize some things. We can't visualize other things.

Einstein's abstract, four-dimensional geometry was hard to concretely visualize. It became visualizable through mathematical relations. When relativity suddenly appeared, it must have seemed to many people: What happened to "real" time? What happened to "real" space? It just got mixed up into this funny thing, but there were rules. The point was there were clear and precise mathematical rules that had been abstracted out of it, and these survived, and the old notions of reality went away.

So I say, let's get rid of the word "reality." Let's have our whole discussion without the word "reality." It gets in the way. It conjures up things that are rarely helpful. The word "reproducible" is a more useful word than "real."

What about quantum mechanics? According to that theory, kicking the same rock the same way can actually give different results.

That's the big one, isn't it? There are two things that were discovered in quantum mechanics that upset our classical sense of reality. One was entanglement. What entanglement said was something very bizarre: that you can know everything there is to know about a composite system and yet not know everything about the individual constituents. It is a good example of how we're simply not biologically equipped for abstraction and how our sense of reality gets upset [see "Living in a Quantum World," by Vlatko Vedral; SCIENTIFIC AMERICAN, June].

The other thing that really hit hard on the idea of classical reality was the Heisenberg uncertainty principle. If you try to describe an object as having both a position and a momentum, you'll run into trouble. You should think of it as having a position or a momentum. Don't try to do both.

This is what physicists mean by "complementary"?

Exactly. It turns out that the mathematics of the event horizon of a black hole is very similar to the uncertainty principle. Again, it's a question of "or" versus "and." At a completely classical level something falls into a black hole, something doesn't fall into a black hole, whatever. There are things outside the black hole, and there are things inside the black hole. What we learned is that's the wrong way to think. Don't try to think of things happening outside the horizon and things happening inside the horizon. They're redun-

Black holes reveal the limits of our capacity to understand the universe.

DON DIXON

dant descriptions of the same thing. You describe it one way, or you describe it the other way. This means we have to give up the old idea that a bit of information is in a definite place [see "Black Holes and the Information Paradox," by Leonard Susskind; SCIENTIFIC AMERICAN, April 1997].

If I get you correctly, the holographic principle extends the complementary model of a black hole to the universe.
Yes. Suppose we want to describe some system with enormous precision. To probe with great precision, you need high energy. What's eventually going to happen as you try to get more and more precise is you're going to start creating black holes. The information in a black hole is all on the surface of the black hole. So the more and more refined description you make of a system, you will wind up placing the information at a boundary.

There are two descriptions of reality: either reality is the bulk of spacetime surrounded by the boundary, or reality is the area of the boundary. So which description is real? There is no way to answer that. We can either think of an object as an object in the bulk space or think of it as a complicated, scrambled collection of information on the boundary that surrounds it. Not both. One or the other. It's an incredibly scrambled mapping of one thing to the other thing.

The original goal of string theory was to provide a unique explanation of reality. Now it gives us multiple universes. What happened?
A large fraction of the physics community has abandoned trying to explain our world as unique, as mathematically the only possible world. Right now the multiverse is the only game in town. Not everybody is working on it, but there is no coherent, sharp argument against it.

In 1974 I had an interesting experience about how scientific consensus forms. People were working on the as yet untested theory of hadrons [subatomic particles such as protons and neutrons], which is called quantum chromodynamics, or QCD. At a physics conference I asked, "You people, I want to know your belief about the probability that QCD is the right theory of hadrons." I took a poll. Nobody gave it more than 5 percent. Then I asked, "What are you working on?" QCD, QCD, QCD. They were all working on QCD. The consensus was formed, but for some odd reason, people wanted to show their skeptical side. They wanted to be hard-nosed. There's an element of the same thing around the multiverse idea. A lot of physicists don't want to simply fess up and say, "Look, we don't know any other alternative."

The universe is very, very big. Empirically we know it's at least 1,000 times bigger in volume than the portion that we can ever see. The success of the concept of cosmic inflation opens the possibility that the universe is varied on big-enough scales. String theory provides Tinkertoy elements that can be put together in an enormous number of ways. So there's no point in looking for explanations of why our piece of the world is exactly the way it is because there are other pieces of the world that are not exactly the same as ours. There can't be a universal explanation of everything that it is any more than there can be a theorem that says the average temperature of a planet is 60 degrees Fahrenheit. Anyone who tried to make a calculation to prove that planets have a temperature of 60 degrees would be foolish because there are lots of planets out there that don't have that temperature.

But nobody knows the underlying rules for multiverses. It's a picture. Nobody knows how to use this predictively. This process of eternal inflation just produces bubble after bubble after bubble and produces any number of them of every kind. So that means that the probability for one versus the other is infinity over infinity. We would like to have a probability distribution that would say one is more probable than the other and then make a prediction. So we've gone from what looks like a very compelling picture on the one hand to absurdly trying to measure an infinity of probabilities. If it's going to go down, it's going to go down because of that [see "The Inflation Debate," by Paul J. Steinhardt; SCIENTIFIC AMERICAN, April].

Is it possible to do theoretical physics and not have philosophical thoughts?
Most great physicists have had a fairly strong philosophical side. My friend Dick Feynman hated philosophy and hated philosophers, but I knew him well, and there was a deep philosophical side to him. The problems that you choose to think about are conditioned by your philosophical predispositions. But I also have a strong sense that surprises happen and put your philosophical prejudices on their head. People have the idea that there are cut-and-dried rules of science: you do experiments, you get results, you interpret them; in the end, you have something. But the actual process of science is as human and as chaotic and as contentious as anything else. SA

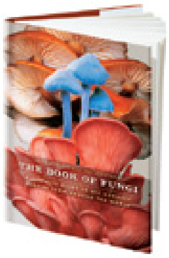
Peter Byrne *is author of "The Many Worlds of Hugh Everett" in the December 2007 issue of* Scientific American, *which developed into the book* The Many Worlds of Hugh Everett III: Multiple Universes, Mutual Assured Destruction and the Meltdown of a Nuclear Family *(Oxford University Press, 2010).*

MORE TO EXPLORE

Farewell to Reason. Paul Feyerabend. Verso, 1988.
The Cosmic Landscape: String Theory and the Illusion of Intelligent Design. Leonard Susskind. Back Bay Books, 2006.
The Black Hole War: My Battle with Stephen Hawking to Make the World Safe for Quantum Mechanics. Leonard Susskind. Back Bay Books, 2009.

SCIENTIFIC AMERICAN ONLINE
Do you think we can grasp reality? Join the discussion at **ScientificAmerican.com/jul2011/susskind**

Recommended by Kate Wong

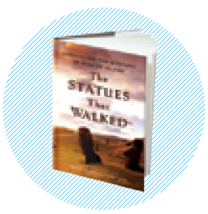


The Book of Fungi: A Life-Size Guide to Six Hundred Species from Around the World

by Peter Roberts and Shelley Evans. University of Chicago Press, 2011 ($55)

Medusa brittlestem, hawthorn twiglet, olive earthtongue—welcome to the weird and wonderful world of fungi, where the species have names that sound as though they could have been plucked from the pages of Harry Potter. Gorgeous color photographs, handy distribution maps and chatty descriptions celebrate edible and poisonous fungal varieties from around the globe.

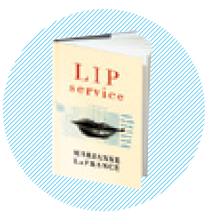
Lion's mane
(actual size)



Statues That Walked: Unraveling the Mystery of Easter Island

by Terry Hunt and Carl Lipo. Free Press, 2011 ($26)

Recent discoveries suggest that the inhabitants of Easter Island were actually devoted stewards of their island's natural resources. Archaeologists Terry Hunt and Carl Lipo describe how they solved the mystery of the society's collapse.



Lip Service: Smiles in Life, Death, Trust, Lies, Work, Memory, Sex and Politics

by Marianne LaFrance. W. W. Norton, 2011 ($26.95)

There are many kinds of smiles, from knowing and joyful to pleading and fake. Smile expert Marianne LaFrance of Yale University discusses the latest science and shows that there is much more to a pair of upturned lips than meets the eye.

The End of Country

by Seamus McGraw. Random House, 2011 ($26)

Journalist Seamus McGraw tells the story of what happened to a small town in rural Pennsylvania after one of the richest natural gas deposits on earth—the Marcellus shale deposit—was discovered there. McGraw's own mother was among the first residents to receive an offer from the gas company to lease her property.

Eruptions That Shook the World

by Clive Oppenheimer. Cambridge University Press, 2011 ($30)

Volcanologist Clive Oppenheimer of the University of Cambridge surveys the biggest eruptions of the past quarter of a billion years to illustrate how profoundly volcanoes have shaped our world and how we might apply the lessons of the past to managing disastrous eruptions in the future.

ALSO NOTABLE

FICTION

Heaven's Shadow, by David S. Goyer and Michael Cassutt. Ace, 2011 ($25.95)

Abyss, by David Hagberg. Forge, 2011 ($24.99)

Rule 34, by Charles Stross. Ace, 2011 ($25.95)

The Silicon Jungle: A Novel of Deception, Power, and Internet Intrigue, by Shumeet Baluja. Princeton University Press, 2011 ($27.95)

FOR KIDS

Me … Jane, by Patrick McDonnell. Little, Brown, 2011 ($15.99)

The Lucy Man: The Scientist Who Found the Most Famous Fossil Ever! by CAP Saucier. Prometheus, 2011 ($16)

Storm Runners, by Roland Smith. Scholastic, 2011 ($16.99)

The Geek Dad's Guide to Weekend Fun: Cool Hacks, Cutting-Edge Games, and More Awesome Projects for the Whole Family, by Ken Denmead. Gotham Books, 2011 ($18)

The Klutz Guide to the Galaxy, by Pat Murphy and the Scientists of Klutz Labs. Klutz, 2011 ($19.99)

TAYLOR LOCKWOOD

COMMENT AT ScientificAmerican.com/jul2011

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

The Believing Brain

Why science is the only way out of the trap of belief-dependent realism

Was President Barack Obama born in Hawaii? I find the question so absurd, not to mention possibly racist in its motivation, that when I am confronted with "birthers" who believe otherwise, I find it difficult to even focus on their arguments about the difference between a birth certificate and a certificate of live birth. The reason is because once I formed an opinion on the subject, it became a belief, subject to a host of cognitive biases to ensure its verisimilitude. Am I being irrational? Possibly. In fact, this is how most belief systems work for most of us most of the time.

We form our beliefs for a variety of subjective, emotional and psychological reasons in the context of environments created by family, friends, colleagues, culture and society at large. After forming our beliefs, we then defend, justify and rationalize them with a host of intellectual reasons, cogent arguments and rational explanations. Beliefs come first; explanations for beliefs follow. In my new book *The Believing Brain* (Holt, 2011), I call this process, wherein our perceptions about reality are dependent on the beliefs that we hold about it, belief-dependent realism. Reality exists independent of human minds, but our understanding of it depends on the beliefs we hold at any given time.

I patterned belief-dependent realism after model-dependent realism, presented by physicists Stephen Hawking and Leonard Mlodinow in their book *The Grand Design* (Bantam Books, 2011). There they argue that because no one model is adequate to explain reality, "one cannot be said to be more real than the other." When these models are coupled to theories, they form entire worldviews.

Once we form beliefs and make commitments to them, we maintain and reinforce them through a number of powerful cognitive biases that distort our percepts to fit belief concepts. Among them are:

ANCHORING BIAS. Relying too heavily on one reference anchor or piece of information when making decisions.

AUTHORITY BIAS. Valuing the opinions of an authority, especially in the evaluation of something we know little about.

BELIEF BIAS. Evaluating the strength of an argument based on the believability of its conclusion.

CONFIRMATION BIAS. Seeking and finding confirming evidence in support of already existing beliefs and ignoring or reinterpreting disconfirming evidence.

On top of all these biases, there is the in-group bias, in which we place more value on the beliefs of those whom we perceive to be fellow members of our group and less on the beliefs of those from different groups. This is a result of our evolved tribal brains leading us not only to place such value judgment on beliefs but also to demonize and dismiss them as nonsense or evil, or both.

Belief-dependent realism is driven even deeper by a meta-bias called the bias blind spot, or the tendency to recognize the power of cognitive biases in other people but to be blind to their influence on our own beliefs. Even scientists are not immune, subject to experimenter-expectation bias, or the tendency for observers to notice, select and publish data that agree with their expectations for the outcome of an experiment and to ignore, discard or disbelieve data that do not.

This dependency on belief and its host of psychological biases is why, in science, we have built-in self-correcting machinery. Strict double-blind controls are required, in which neither the subjects nor the experimenters know the conditions during data collection. Collaboration with colleagues is vital. Results are vetted at conferences and in peer-reviewed journals. Research is replicated in other laboratories. Disconfirming evidence and contradictory interpretations of data are included in the analysis. If you don't seek data and arguments against your theory, someone else will, usually with great glee and in a public forum. This is why skepticism is a sine qua non of science, the only escape we have from the belief-dependent realism trap created by our believing brains.

COMMENT ON THIS ARTICLE ONLINE
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Illustration by Richard Mia

Steve Mirsky has been writing the Anti Gravity column since he was a man trapped in the body of a slightly younger man. He also hosts the *Scientific American* podcast Science Talk.

Rules of the Road

Knowing the laws of persuasion is especially handy with car dealers

It served nobly, though it was not a Plymouth Valiant. It took me to new places, though it was not a Ford Explorer. I parked it under a tree, though it was not a Toyota Sequoia. (The tree was a maple.) It was the last car I had bought, a 1992 Honda Civic. It even had *an* air bag—for the driver. But the years had passed it by: my passengers wanted air bags, too, and I conceded that it was time for a new car.

Also, the air conditioner has been busted for something like eight years. I frequently considered rectifying the situation, but it seemed like a poor investment to throw $1,000 into a car with a book value of, well, nothing. The economics of such a repair said that I wouldn't be making an air-conditioned car, I'd be making a portable air conditioner.

So I entered the automobile market. Which meant interacting with one of the most lampooned and reviled figures in the history of American commerce: the car salesman. Fortunately, I walked into showrooms armed. Because I had read *Scientific American*'s February 2001 article by social psychologist Robert B. Cialdini, "The Science of Persuasion." The piece outlines the basic methods to change someone's mind or to get the person to act a certain way. And knowing about these methods can offer immunity to the one being persuaded—aka the mark or the chump.

For example, when the chatty salesman at the first dealership discovered, or invented, that we had similar backgrounds, I knew that he was trying to establish rapport, because we are much more likely to do something for somebody we like. It didn't work.

When he called a few days later to tell me that the car I had looked at was available at a reduced price "today only," I knew that he was using the scarcity tactic—we're more enticed to grab something when its availability is limited. This approach might have paid off if the car he was selling wasn't also limited in its right-side sight lines. At the "today only" price, it was an attractive option if I committed to making only left turns.

The salesman at a second dealership sat next to me on a test drive. As we passed a gas station, he said, "Whew, look at those prices." I realized that this remark was a reminder that the car would use less high-cost fuel. As social creatures, humans are hardwired to reciprocate when someone does something for us. And he was allegedly doing me the favor of saving money on gas in the future, making me more likely to do him the favor of buying his car in the present. His theoretical generosity was sadly mitigated by the car being a kidney-rattling tin can.

At the third dealership, I encountered a laid-back salesman whose style actually did make me like him, whether that was his strategy or not. I also liked his car and bought it. But when I went to take delivery, I was disappointed to find that the brand-new car had a long and ugly scratch on the hood. My salesman was out that day, and I was told I would have to talk to the business manager. He sat on a platform two feet above the showroom floor. This move, of course, is designed to make him appear to be an authority figure—all he needed was the black robe and gavel—because we are inherently moved to believe in and submit to authority.

Again, my knowledge offered me some immunity. When I told the business manager that I would not be accepting the car until the scratch was dealt with, he invoked the rules of reciprocity and scarcity: "You know," he said, "we worked really hard to get you this car." I then countered with my own scarcity move—I pulled the check out of my pocket and said, "Well, I worked really hard for this money. Call me when the car is perfect."

Which they did the very next day. Of course, we both know that I didn't really work hard. But that can be our little secret. Because we're friends, right?

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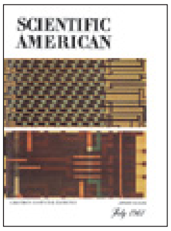
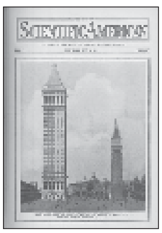
Illustration by Matt Collins



July 1961

Forecasting Revolution

"The behavior of the atmosphere is so complex that it was not to be expected that a few months of satellite observation would suddenly clarify weather processes or lead to an immediate improvement in forecasts. Nevertheless, meteorologists who have been following the data received from *Tiros I* and *Tiros II* are convinced that weather satellites will have a revolutionary impact on their science. Because of this conviction, an enlarged series of weather satellites is being planned by the U.S. Weather Bureau in co-operation with the National Aeronautics and Space Administration."



July 1911

Cancer's Roots

"It is now scarcely ten years since the experimental investigation of the cancer problem was first entered upon, and therefore we are today only on the threshold of a true and definite knowledge regarding cancer. Modern experimental investigation has not as yet shown the cause of cancer. It has, however, definitely shown that the problem of cancer is intimately related to the problem of cell growth, and it is along this line that future work must be directed. As to whether the primary cause of cancer be a micro-organism or whether we must look to some change in the nature or function of the cell itself for the explanation of the origin of cancer, we are not in a position to state."

Swift Incompletion

"Upon the departure of the huge 'Olympic' on her first eastern trip from New York on June 28th, Aviator Tom Sopwith attempted to drop a message on board the steamer when she was passing through the Narrows. He flew down to within 200 feet of her before dropping the package. This missed the deck by a few feet and was lost in the bay. Nevertheless, the possibilities of the aeroplane for delivering mail were demonstrated in a practical way."

Soylent Tabby?

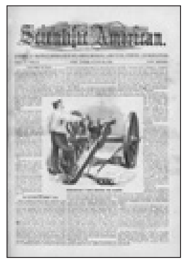
"Snails are now being sold in Paris, the only genuine part of which are the shells. It is said that the imitation of the real article is so close that many epicures have a high opinion of the sham product. Snail-shells, it seems, are bought from the dustmen and rag-pickers, and after being cleaned are filled with 'lights' or cats' meat, the soft flesh being cut into corkscrew form, so as to fit the shell, by a skillfully designed machine. The receptacle is then sealed with liquid fat, and the *escargot* is ready for the consumer. The secret came out during a lawsuit brought by a man employed at the snail-factory to recover damages for a finger mutilated by one of the machines."

Our Merchant Marine

"The Panama Canal is nearing completion. As it appears now, all the countries that control a merchant marine will be in a position at once to make use of this new maritime route. Our country, however, has taken no steps to the same end, but on the contrary our strength is dissipated in discussions about ways and means by which the merchant marine might be restored [*see illustration*]. It looks to me that this delay may have serious consequences. We not only lose the immediate opportunity and profit; but routes once established and connections made by foreign trade are not easily dislodged. We should be prepared at the inception to take full advantage of this route, established by our enterprise and with our money."

The American Merchant Marine: a call for expansion of the civilian shipbuilding industry, 1911

SCIENTIFIC AMERICAN, VOL. CV, NO. 3; JULY 15, 1911



July 1861

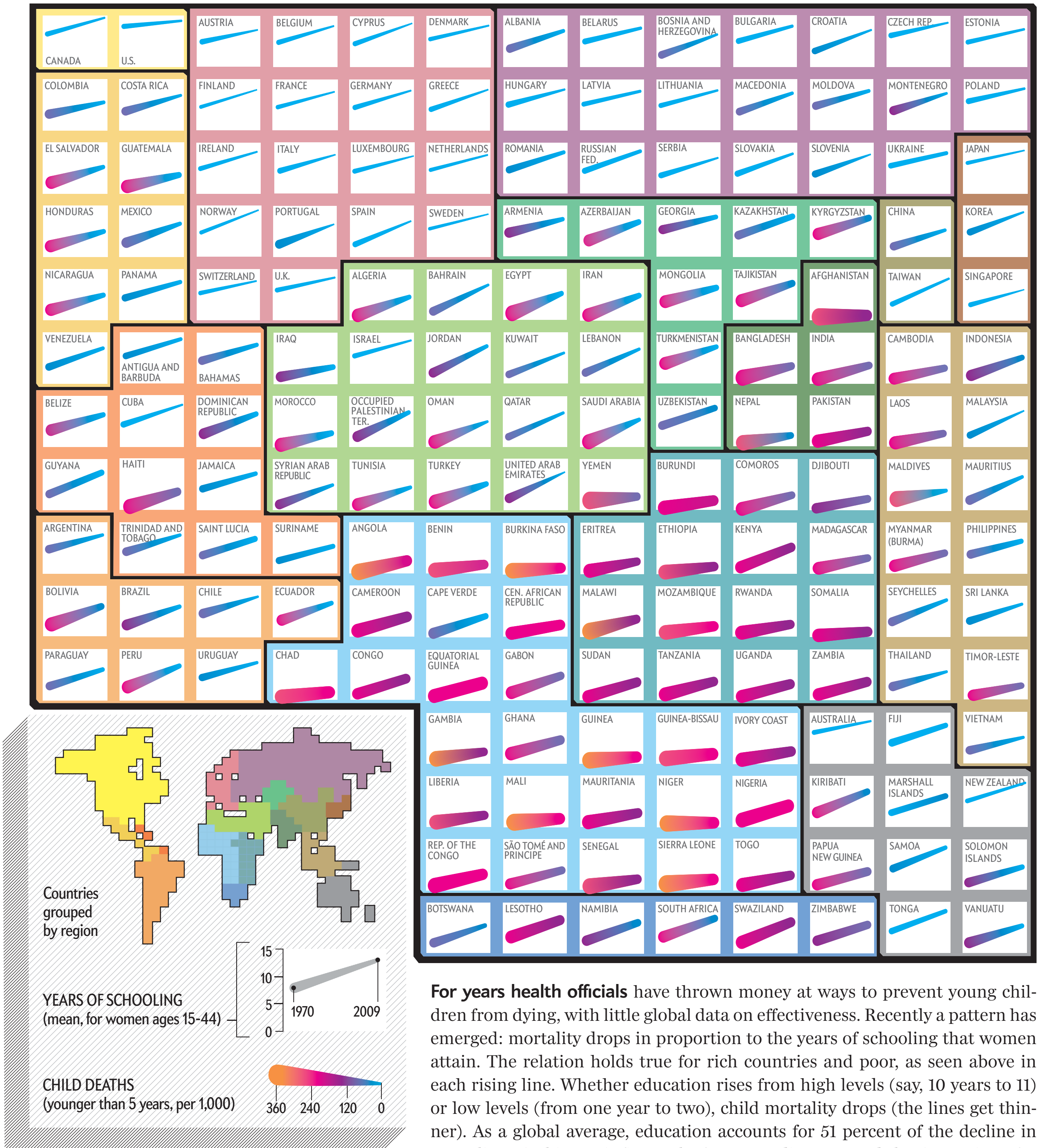
Malaria and War

"It is difficult for us to realize the fact, but we all know that any soldier is in five times more danger of dying from malarious disease than of being killed in battle. What malaria is nobody knows. It may consist of organisms, either animal or vegetable, too minute for even the microscope to detect; or it may be some condition of the atmosphere in relation to electricity, or temperature, or moisture; or it may be a gas evolved in the decay of vegetable matter. The last is the most common hypothesis, but it is by no means proved, and it has some stubborn facts against it. There is no doubt, however, that malaria is some mysterious poison in the atmosphere, and that it is confined strictly to certain localities. All experience has confirmed the observation of the natives of Peru, that Peruvian bark has a powerful influence in counteracting the poison in malaria. We advise all of our soldiers to consult the surgeons of their several regiments in regard to the wisdom of this course, and to follow it resolutely."

Full article is available at www.ScientificAmerican.com/jul2011/quinine

Baby's Life, Mother's Schooling

Child mortality rates decline as women become better educated



SCIENTIFIC AMERICAN ONLINE
More data at ScientificAmerican.com/jul2011/graphic-science

For years health officials have thrown money at ways to prevent young children from dying, with little global data on effectiveness. Recently a pattern has emerged: mortality drops in proportion to the years of schooling that women attain. The relation holds true for rich countries and poor, as seen above in each rising line. Whether education rises from high levels (say, 10 years to 11) or low levels (from one year to two), child mortality drops (the lines get thinner). As a global average, education accounts for 51 percent of the decline in mortality—the biggest influence by far—according to a study by the Institute for Health Metrics and Evaluation. Educated women, it seems, make wiser choices about hygiene, nutrition, immunization and contraception. —*Mark Fischetti*

SOURCE: UNIVERSITY OF WASHINGTON'S INSTITUTE FOR HEALTH METRICS AND EVALUATION

Graphic by Joshua Korenblat and Jen Christiansen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LINCOLN
*The Lincoln MKZ received the lowest number of problems per 100 vehicles among entry premium cars in the proprietary J.D. Power and Associates 2010-2011 Vehicle Dependability Studies.℠ 2011 study based on 43,779 consumer responses measuring problems consumers experienced in the past 12 months with three-year-old vehicles (2008 model-year cars and trucks). Proprietary study results are based on experiences and perceptions of consumers surveyed October-December 2010. Your experiences may vary. Visit jdpower.com.